

RISK FACTORS AFFECTING QUALITY OF LIFE IN A GROUP OF ITALIAN CHILDREN WITH ASTHMA

L. INDINNIMEO¹, F. CHIAROTTI², V. DE VITTORI¹, L. BALDINI³, G. DE CASTRO¹,
A.M. ZICARI¹, G. TANCREDI¹, L. LEONARDI¹ and M. DUSE¹

¹Center of Pediatric Immunology and Allergology, Umberto I Hospital, Sapienza University of Rome, Rome, Italy; ²Department of Cellular Biology and Neuroscience, Istituto Superiore di Sanità, Rome, Italy; ³Department of Psychology of the Processes of Development and Socialization, Sapienza University of Rome, Rome, Italy

Received January 22, 2014 – Accepted April 30, 2014

The measure of Quality of Life (QoL) has become one of the most important criteria used to assess the impact of chronic illness, such as asthma, on the patient's daily life, in adults and children alike. The objective of our open observational study was to measure the QoL and analyze several factors that potentially affect QoL, such as symptoms and functional respiratory parameters, in a cohort of children with asthma. One hundred and twenty-seven children with asthma, 6 to 14 years of age, living in the city of Rome, were enrolled as outpatients. They were subjected to Skin Prick Tests (SPT), underwent spirometry and filled out the Pediatric Asthma Quality of Life Questionnaire (PAQLQ). One hundred and eleven children were diagnosed with intermittent asthma, 12 (10%) with mild asthma, and four with moderate persistent asthma. Ninety-six children had a positive SPT. The mean total score of QoL, obtained from the questionnaire, was 5.4 (± 1.2 SD). Two QoL groups were created. Children with total QoL score < 5.5 were included in the "Lower QoL" score group while children with total QoL score ≥ 5.5 were included in the "Higher QoL" score group. Children in the Higher group and their mothers had a higher mean age, suffered from fewer asthma exacerbations during the year preceding the study, and showed a higher mean value of forced expiratory volume (FEV1) compared to the children in the Lower category. Using Logistic regression we identified the main factors that may affect QoL as FEV1, symptoms in the previous year and mother's age. QoL is correlated with the frequency of asthma exacerbations and FEV1 values. Furthermore, our research shows that a significant impairment of QoL may also occur in patients with normal lung function, pointing out the importance of evaluating QoL in all children with asthma.

Measures of Quality of Life (QoL) indicate how much an illness interferes with an individual's daily activities and how well the patient is adapting to his/her illness across several areas of functioning, such as social limitations, emotional impact, and physical

activities (1). The QoL measure has become one of the most important criteria used to analyze the patient's state of health and the efficacy of therapies. That is why the most up-to-date guidelines and the modern concept of evidence-based medicine

Key words: Quality of life, pediatrics, asthma, FEV1, mothers, questionnaire

Mailing address: Prof. Luciana Indinnimeo,
Policlinico Umberto I,
Sapienza Università di Roma
Viale Regina Elena 328, Roma, Italy
Tel.: +39 06 49979302
Fax: +39 06 49979377
e-mail: luciana.indinnimeo@uniroma1.it

integrate objective parameters with health-related QoL as a subjective parameter (1). This integrated approach has proved so useful in chronic disease management that in recent years, increasingly more detailed questionnaires have been developed to assess the impact of chronic illness on the patient's daily life (2-4).

Asthma is the most common chronic disease in childhood and is a major health problem. Its solutions include developing treatment and follow-up guidelines. To date, in clinical practice, the goals of asthma treatment have been mainly the reduction of symptoms, the improvement of lung function and the decrease in the demand for bronchodilators. Little attention has been paid to functional, physical, emotional and social limitations experienced daily by children with asthma (5-7). Children with partly controlled asthma may have difficulties interacting with peers and performing adequately in sports (8), which results in frustration and discontent (9-10). These issues, fundamental to a balanced mental and physical development, are analysed in QoL evaluation; it is designed to assess how and how much asthma affects patient's daily life (11) and to monitor the effectiveness of the treatment in the perception of both the child and his/her family (12).

The relationship between asthma severity and child QoL is a matter of debate. In some studies, symptoms of poorly controlled asthma, such as wheezing and night-time waking, are not consistently associated with measurements of child QoL (13, 14), whereas other studies report such relationships (15-17). Analysing the relationship between the PAQLQ and lung function, Ricci et al. demonstrated that the PAQLQ does not discriminate QoL in patients with a good lung function (18). A recent review of 14 studies found strong support for asthma severity as a significant correlate of child QoL in pediatric asthma. This review showed that as the severity of the child's asthma worsened, the QoL of the child declined (19). This is consistent with the inverse relationship between asthma severity and QoL among adults with asthma (20).

The PAQLQ has been translated into several languages: its Italian version was proposed in 1999 (21) and the cross-cultural adaptation was made according to the proposed guidelines (22). Using PAQLQ our study aimed to identify potential risk

factors, including symptoms, age of patients and their mothers, and functional respiratory parameters that could have an impact on the daily QoL in a group of children with asthma in Rome.

MATERIALS AND METHODS

Study population

This is an open observational pilot study. Asthmatic children aged 6 to 14 years were consecutively enrolled from March 2010 to June 2010 as outpatients at the Center of Pediatric Immunology and Allergology. Approval was obtained from the Department of Pediatrics, Umberto I Hospital, University of Rome "Sapienza". Parental consent was obtained.

Questionnaires

The enrolled children filled out the Pediatric Asthma Quality of Life Questionnaire (PAQLQ), developed by EF Juniper et al. (23). The PAQLQ consists of twenty-three questions, divided into three domains, that were used for QoL assessment:

Symptoms: coughing, wheezing and asthma attacks (10 questions)

Limitations of activities: running, playing (5 questions)

Emotional impact: frustration, fear and irritation (8 questions).

Three of the questions regarding activities are personalized, allowing the children to choose among 34 activities in which asthma limits their performance. Children are also asked to assess how their illness interfered with daily life in the week before completing the questionnaire. The questionnaire uses a 7-point scale (min=1; max=7) for each question. Based on the mean QoL total score found in our sample (5.4 ± 1.2), we categorized children into two subgroups as "Lower" QoL (Total QoL <5.5; n=60) or as "Higher" QoL (Total QoL ≥ 5.5 ; n=67). The higher the score, the lower the influence of asthma on the child's QoL.

In our study, PAQLQ was administered to children under health care supervision, regardless of age.

For younger children (aged from 6 to 8 years), the questionnaire was completed in the presence of their parents in order to make them feel more confident (24). The questionnaires were completed during an outpatient clinic visit before meeting the physician and running spirometry.

The degree of asthma control was assessed by physicians from the Center of Pediatric Immunology and Allergology, according to the Global Initiative for Asthma (GINA) guidelines, which have three asthma levels: controlled, partly controlled, and uncontrolled (25), based

on symptoms, functional respiratory parameters and asthma exacerbations.

Skin prick test

Skin Prick Tests (SPT) for inhalant and food allergens were performed once parents had signed the informed consent. SPT were made using a panel of standardized allergen extracts (Lofarma), including 9 common inhalant allergens such as *Dermatophagoides pteronyssinus*, *Dermatophagoides farinae*, *Alternaria tenuis*, animal fur (including cat and dog epithelia), *Parietaria officinalis*, grass pollens (*Cnodon dactylon* and *Lolium perenne*), *Olea europea*, and food allergens such as milk proteins (*alpha lactalbumin*, *beta lactoglobulin*, casein), egg (yolk and white), fish and wheat. The SPTs were controlled with positive and negative controls (histamine and saline).

Statistical analysis

Quantitative data were synthesized by means [$\pm$ standard deviations (SD)], medians, and ranges (minimum-maximum value). Qualitative data were presented as absolute and percent frequencies. Data were shown for the overall group of children and for subgroups based on sex, on the QoL total score and on the separate scores for each of the following domains: activity, symptoms and emotions. A cut-off value for QoL total score was chosen based on the mean value observed for that variable in the overall group of children; this value is equal to 5.4 (approximation to one digit after the decimal point). Children were then categorized into two subgroups "Lower" QoL score group (total QoL <5.5: n=60) and "Higher" QoL score group (total QoL $\geq$ 5.5: n=67). In the former we put children having a QoL total score less than 5.5 (including children with a QoL total score equal to the observed mean value), while in the latter we put children having a QoL total score greater than or equal to 5.5. The two groups obtained with these criteria, were approximately balanced. The *chi*-square test was used for categorical variables and the non-parametric Mann-Whitney U test was used for quantitative variables.

Multivariate analysis

Multivariate analysis was performed using backward stepwise linear regression and logistic regression (p remove = 0.50, p entry = 0.049). The dependent variable was QoL for the Total score and for the scores in each domain in separate analyses (linear regression: quantitative score; logistic regression: "lower" vs "higher QoL" score groups).

Sex, age of the child and that of his/her mother, number of wheezing attacks in the month preceding the study (NWAm), number of wheezing exacerbations during the year preceding the study (NWAY), and FEV1,

were considered as potential prognostic factors. Although some of the variables, considered as potential independent predictors, were expected to contribute to the child's perception of his/her QoL (e.g. number of wheezing attacks during the month and the year preceding the study), the size of the effect these variables can have on the perceived quality of life is subjective. In addition, no direct information on these variables was included in the PAQLQ. For these reasons, we decided to evaluate their specific effect on QoL scores.

As for linear regression, coefficients with standard error (SE) are shown for the variables included in the final models. Coefficients represent the change in the dependent variable corresponding to a one-unit increase in the independent variable (e.g. increase of one year of age, either for the child or for the mother, of one NWAm, of one NWAY, of 1% of FEV1).

Regarding the variable gender (binary variable), female gender was used as reference group, and the coefficient represents the expected mean change in the dependent variable observed in males compared to females.

Significant negative coefficients (i.e., negative coefficients whose 95% CI lies all under 0) indicate an inverse correlation between the independent variable and the QoL score (the higher the variable, the lower the score), while significant positive coefficients (i.e. positive coefficients whose 95% CI lies all above 0) indicate a direct correlation between the independent variable and the QoL score (the higher the variable, the higher the score).

As for logistic regression, Odds Ratios (ORs) with 95% confidence intervals (95% CIs) are presented for the independent variables included in the final selected model. The OR represents the risk of falling into the "Lower" QoL score group associated to a one-unit increase in the independent quantitative variable. An OR significantly >1 (i.e., an OR whose 95%CI lies all above 1) or an OR significantly <1 (i.e. an OR whose 95%CI lies all under 1), implies that the risk of falling into the "Lower" QoL score group increases, or decreases, upon the variation of the independent variable.

All of the statistical analyses were performed using Stata Statistical Software (StataCorp. 2003. Stata Statistical Software: Release 8.0. College Station, TX: Stata Corporation.).

RESULTS

Population characteristics

We consecutively evaluated 127 children with a history of asthma: 83 of whom were males (65%), and the overall mean age was 9.2 years. One hundred

Table I. Features of the 127 children enrolled.

Features	Total
Participants [n (%)]	127 (100)
Age [mean $\pm$ SD; median (min to max)]	10.4 $\pm$ 2.0 10 (7 to 15)
Age of mother [mean $\pm$ SD; median (min to max)]	40.5 $\pm$ 4.7 40 (31 to 56)
Age of mother at child birth [mean $\pm$ SD; median (min to max)]	30.0 $\pm$ 4.6 29.5 (20 to 47)
Children with Positive SPT [n (%)] ¹	96 (75.6)
Asthma [n (%)] ¹	
Controlled	114 (89.8)
Partly controlled	10 (7.9)
Uncontrolled	3 (2.4)
QoL average score in the domains [mean $\pm$ SD; median (min to max)]	
Activity	4.9 $\pm$ 1.4 5.2 (1.3 to 7)
Symptoms	5.1 $\pm$ 1.4 5.4 (1.8 to 7)
Emotion	5.8 $\pm$ 1.2 6.3 (2.4 to 7)
Total	5.4 $\pm$ 1.2 5.6 (2.2 to 7)
"Poor" QoL in the domains [n (%)] ²	
Activity	75 (59.1)
Symptoms	67 (52.8)
Emotion	39 (30.7)
Total	61 (48.0)

¹The percentages are computed on the total number of subjects of the same sex groups included in the analysis.

and fourteen children (90%) had controlled asthma, 10 (8%) partly controlled asthma, and 3 (2%) uncontrolled asthma; 96 children had one or more positive SPT. Clinical features are reported in Table I. None of the children had current asthma symptoms at the time of completing the questionnaire. The enrolled children identified the activities of running (21%), climbing stairs (11%), and playing soccer (8%) as those mostly affected by their condition.

QoL mean scores

The average QoL score ($\pm$ SD) measured for the 127 children was 5.4 ($\pm$ 1.2) and the median was 5.5 (range 2.2-7.0).

When the scores of each of the three domains of the QoL were analyzed separately, the lower values were observed in the activity category (mean 4.9 $\pm$ 1.4 and median 5.2, range 1.3-7.0), whereas those in the emotions domain reached the highest values

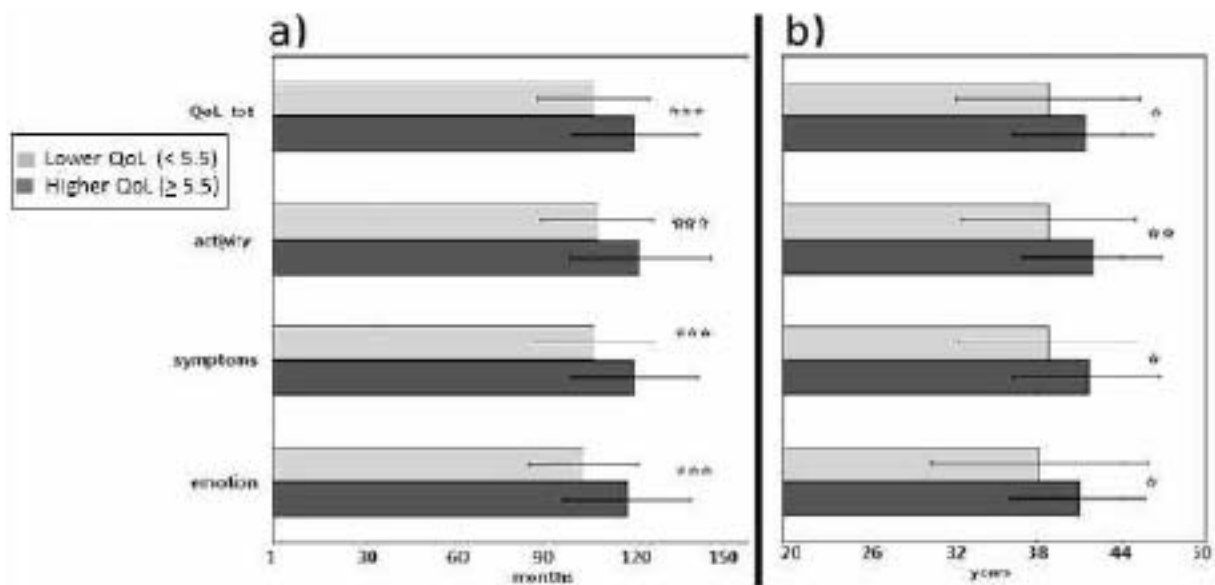


Fig. 1. Mean age of children (a) and of their mothers (b) among the 60 patients with total QoL score < 5.5 (Lower) and the 67 patients with total QoL score ≥ 5.5 (Higher). Children were categorized into two subgroups, “Lower QoL” and “Higher QoL”, on the basis of the mean QoL total Score found in our sample (5.4 ± 1.2).

☆ $p < 0.01$ ☆☆ $p < 0.001$ ☆☆☆ $p < 0.00001$

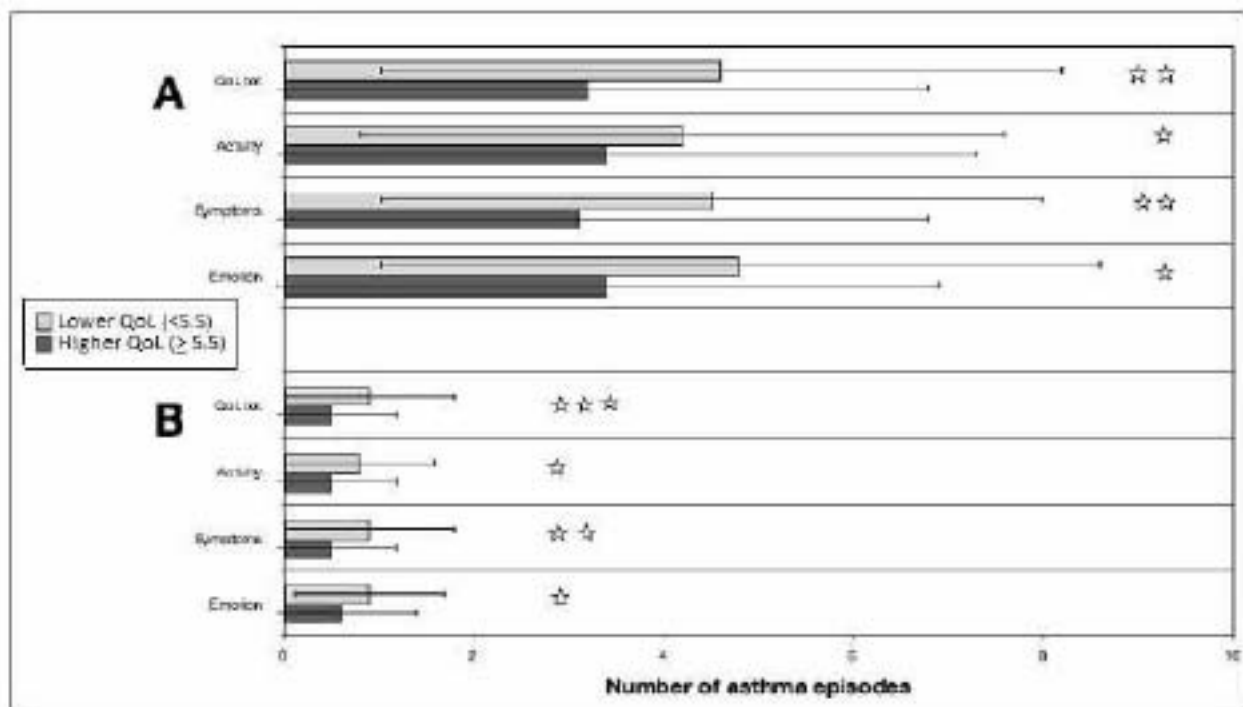


Fig. 2. Number of asthma episodes in the last year (A) and in the last month (B) among the 60 patients with total QoL score < 5.5 (Lower) and the 67 patients with total QoL score ≥ 5.5 (Higher). Children were categorized into two subgroups, “Lower QoL” and “Higher QoL”, on the basis of the mean QoL total Score found in our sample (5.4 ± 1.2).

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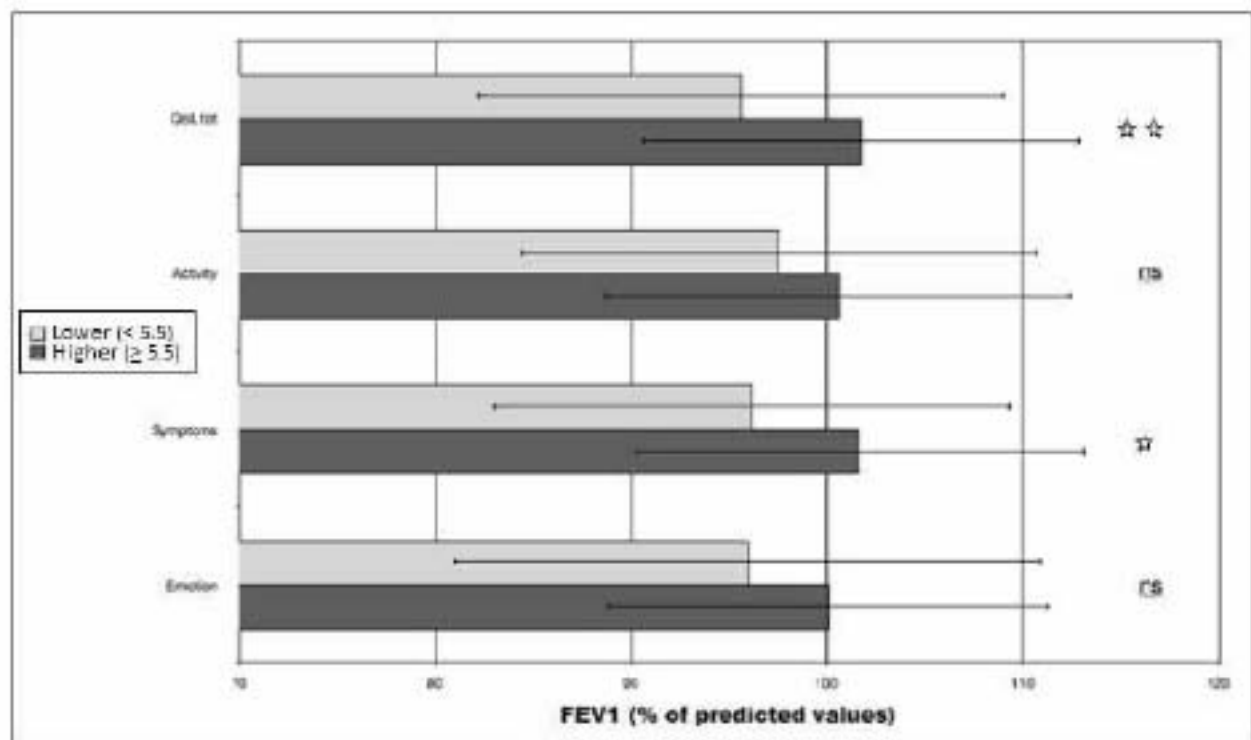


Fig. 3. Mean FEV1 values among the 60 patients with total QoL score < 5.5 (Lower) and the 67 patients with total QoL score ≥ 5.5 (Higher). Children were categorized into two subgroups, “Lower QoL” and “Higher QoL”, on the basis of the mean QoL total Score found in our sample (5.4 ± 1.2).

☆ $p < 0.01$ ☆☆ $p < 0.001$

(average 5.8 ± 1.2 and median 6.3, range 2.4-7.0).

QoL and lung function, asthma severity and age

The children in the “Higher QoL” group and their mothers had a higher mean age compared to children and mothers in the “Lower QoL” category. Both differences were found to be significant (Fig. 1). Moreover, out of the 127 patients enrolled in the study, children in the higher QoL reported fewer asthma exacerbations during the year preceding the study (Fig. 2) and showed a higher mean value of FEV1, expressed as a percentage (Fig. 3).

These results were confirmed also by a multivariate analysis. Linear regression showed that the factors significantly associated with the QoL score, either for total QoL or for the separate domains, were FEV1 (the higher FEV1, the higher the QoL score) and wheezing exacerbations in the previous year (the higher the number of wheezing exacerbations, the lower the QoL score). QoL score for the symptoms

domain changed significantly according to the number of wheezing attacks in the previous month (the higher the number, the lower the QoL score) (Table IIa). Similarly, logistic regression showed that the main factors significantly associated to the QoL were FEV1, symptoms in the previous month or year, and mother’s age (Table IIb). Specifically, any increase of one unit in FEV1 decreased the risk of falling into the “Lower QoL” score group by about 70-80%, both in total score and in the scores of the individual domains. The risk of falling into the “Lower QoL” score group significantly increased, up to more than two-fold, both for Total and Symptoms domain, for any more wheezing attacks in the month preceding the study. The risk increased by about 20% in the Emotion domain for any more wheezing attacks in the year preceding the study. The risk increased by about 20% in the Emotion domain for any more wheezing attacks in the year preceding the study. Finally, for the Activity and Symptoms

Table II. Linear and logistic regression analysis results.

<i>a) Linear regression</i>						
Domain	Variable	Coeff	SE	t	P	95%CI
Total QoL	FEV1 (% of predicted values)	0.79	0.213	3.72	<0.001	0.37 to 1.21
	Asthma last year	-0.13	0.033	-3.83	<0.001	-0.19 to -0.06
Activity	FEV1 (% of predicted values)	0.69	0.245	2.84	0.006	0.21 to 1.18
	Asthma last year	-0.13	0.038	-3.33	0.001	-0.20 to -0.05
Symptoms	FEV1 (% of predicted values)	0.84	0.231	3.63	<0.001	0.38 to 1.30
	Asthma last year	-0.10	0.042	-2.39	0.019	-0.18 to -0.02
	Asthma last month	-0.42	0.178	-2.34	0.022	-0.77 to -0.06
Emotion	FEV1 (% of predicted values)	0.72	0.216	3.34	0.001	0.29 to 1.15
	Asthma last year	-0.10	0.034	-2.98	0.004	-0.17 to -0.03

<i>b) Logistic regression</i>						
Domain	Variable	OR	SE	Z	P	95%CI
Total QoL	FEV1 (% of predicted values)	0.18	0.095	-3.30	0.001	0.07 to 0.50
	Asthma last month	2.34	0.761	2.61	0.009	1.24 to 4.43
Activity	FEV1 (% of predicted values)	0.30	0.143	-2.54	0.011	0.12 to 0.76
	Mother's age	0.90	0.043	-2.08	0.037	0.82 to 0.99
Symptoms	FEV1 (% of predicted values)	0.22	0.112	-2.97	0.003	0.08 to 0.60
	Asthma last month	2.01	0.649	2.15	0.031	1.06 to 3.78
	Mother's age	0.90	0.046	-2.04	0.041	0.81 to 0.99
Emotion	FEV1 (% of predicted values)	0.24	0.132	-2.60	0.009	0.08 to 0.70
	Asthma last year	1.18	0.088	2.28	0.023	1.02 to 1.37

domains, the risk of falling into the "Lower QoL" score group significantly decreased by about 10% for any one-year increase in the mother's age.

As for FEV1, no significant difference was observed between the 57 children (45%) who did not receive treatment and the 70 children (55%) who received treatment with one or more drugs (inhaled corticosteroids, antileukotrienes, long-acting beta agonists) at the time the questionnaires were completed ($p > 0.5$). The majority of children had FEV1 values in the normal range (26)

QoL and gender

Gender was not correlated significantly with the QoL scores in our study. Only for the emotion domain, the proportion of females with a Lower QoL was significantly higher than that of males (43.2% vs 24.1%, $p = 0.027$).

DISCUSSION

Our study demonstrates a highly significant correlation between respiratory function values and QoL in children with asthma in Rome. Logistic regression reveals that children with greater levels of QoL have higher FEV1 values. The correlation becomes even more noteworthy if we consider that the majority of children who took part in the study suffer from controlled asthma, some without therapy and others with the appropriate therapy, with FEV1 values nearly within the normal range. Results revealed that QoL was significantly correlated with respiratory performance, even when participants had a normal lung function. These results contradict those obtained by Ricci et al. (18) which show that the PAQLQ does not discriminate QoL in patients with a good lung function, with a plateau of the

FEV1 results over the 60th percentile. Multiple linear regression performed on QoL scores gave results consistent with those of logistic regression applied to dichotomized QoL data.

Rydström et al. studied the QoL in 225 Swedish children with mild asthma, but did not perform spirometry (27). They found lower scores of QoL in the activity domain compared to the symptom and emotion domains, but could not provide a correlation with FEV1. In a cross-sectional study, Hallstrand et al. assessed QoL of 160 adolescent athletes with the teen version of the pediatric quality-of-life inventory (PedsQL™) and performed spirometry before and after an exercise challenge test (28). Young athletes with a previous diagnosis of asthma showed a lower quality of life than peers who had never been diagnosed with asthma. However, the sample was too small to allow the authors to correlate QoL, asthma and spirometry.

Furthermore, in our study, QoL seems to be correlated to the seriousness of asthma: children reported progressively lower QoL scores – both as total and single domains – in cases where asthma exacerbations were more numerous in the previous month and year (29).

Regarding the assessment of activities selected by the children as ones largely compromised by asthma, “running” is the most frequently reported, a finding that is in agreement with other observations (30, 31). Running is a fundamental aspect of most children’s games and sports and it is easy to understand that the child who is unable to participate in group activities feels different and frustrated. This significantly impinges on their self-esteem (9, 10).

The Emotion domain of QoL in females shows a risk of falling into the “Lower QoL” category by a factor of approximately 2.5 when compared to males. A study linking health disadvantage with gender supports these claims; it showed that the majority of girls incorporated their conditions and the associated treatment regimens into their social and personal identities. This could have detrimental effects in terms of control, as girls sometimes lower their expectations (32).

Finally, our study points out that QoL scores, both total and single domain scores and especially Activity domain scores, improve as the age of children and of their mothers increases (33), as already described

by Rydstrom et al. (27). A possible explanation is that older children are more aware of their illness and can better manage it, and older mothers become more practical and experienced. Furthermore, older mothers instil greater confidence in their children, encouraging them to participate in activities with their peers (27, 34). The principal limitation of this study is the small number of participants selected from a single outpatient setting. Consequently, we are unable to make generalizations about the findings of this study. Furthermore, we did not take into account the relationship between QoL and the socioeconomic status of families who have children with asthma.

In conclusion, after analyzing multiple possible risk factors related with QoL, including demographics, asthma severity, and lung function our study shows that the frequency of asthma exacerbations influences QoL, that is correlated with FEV1 values, even when the variations are near the lower limits of the normal range.

These results point out the importance of assessing QoL through reliable and specific tools in the management of all children with asthma, including those with lung function near the normal range. This could allow physicians to identify the patients with an increased risk of having a worse QoL, in order to provide them with effective assistance and support and maintain the child’s overall well-being.

ACKNOWLEDGEMENTS

All the authors thank Russ Manitt, Ph. D, Postdoctoral Fellow of Harvard University, for the final copy editing of the manuscript.

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