Original article

Health-related quality of life assessment using EQ-5D-Y questionnaire in a group of Egyptian asthmatic children

Background: *Asthma, as a common chronic illness, negatively influences children's quality of life. We sought to investigate the health-related quality of life (HRQoL) in a sample of Egyptian asthmatic children.* ***Methods:*** *A cross-sectional study was conducted in the Pediatric Allergy and Immunology Unit of Ain Shams University, including three groups of age and gender-matched children, aged 6-12 years; an asthma group (n=100), non-asthmatic group with respiratory tract infections (n=114), and a healthy control group (n=100). The EQ-5D-Y questionnaire was used to evaluate the HRQoL in each study group. This questionnaire also comprises a visual analogue scale (VAS) which is scored from zero (worst) to 100 (best) as judged by the patient.* ***Results:*** *HRQoL assessment revealed that 86% of the asthmatic children faced problems with their daily activities, 43 % had worries, sadness and unhappiness and 22% had mobility problems (walking around). Thirteen percent of the cases expressed some pain or discomfort due to their disease, while self-care was the least affected (6%). Parameters of mobility, doing usual activities, feeling worried or sad were more frequently affected among the asthmatics in comparison to the other two groups (X2 = 37.02, 46.38, 22.90, respectively with p <0.001). Enrolled asthmatic children showed the lowest values of visual analogue scale (VAS) scores (mean ± SD: 72.2 ± 24.6) in comparison to the infection and healthy control groups (mean ± SD: 84.6 ± 12, 92.8 ± 9.6, respectively; f = 39.03; p value = 0.001).* ***Conclusion:*** *Asthma has a significant adverse impact on HRQoL of children and the EQ-5D-Y questionnaire could be an applicable instrument to measure their quality of life.*

Keywords: Asthma, children, EQ-5D-Y, GINA, quality of life, visual analogue scale.

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INTRODUCTION

Quality of life is defined as the perception that individuals have of their position in life, in the context of the culture and system of values in which they live and in relation to their objectives, expectations, standards, and concerns. Quality of life can change according to the environment and the experiences, as well as in response to certain diseases.[1]

Asthma is a common chronic health care problem in children and adolescents[2] Current clinical practice guidelines emphasize that the overall goal of asthma management is to achieve asthma control.[3] The quality of life of children and adolescents with asthma deserve special attention, because asthma affects not only the individuals with the disease, but also their caregivers, thereby altering the family's normal life activities.[4]

We sought to investigate the health-related quality of life (HRQoL) in a group of asthmatic children in relation to their asthma severity and symptom control. We used the EQ-5D-Y questionnaire, which is a generic, youth-specific and age-appropriate measure of HRQoL. In comparison to other questionnaires, EQ-5D-Y questionnaire is relatively short, easy and quick to fill, with age-appropriate wording and a short recall period and time frame to avoid comprehension and memory problems.[5] The questionnaire has already proved its applicability in various indications and populations.[6,7] This questionnaire also comprises a visual analogue scale (VAS) which is scored from zero (worst) to 100 (best) as judged by the patient.

METHODS

Study design: We conducted an observational, cross-sectional, analytical study that was carried out at the Pediatric Allergy and Immunology unit,

Children's Hospital, Ain Shams University during the period from April 2018 to May 2019.

Study subjects: The study included three gender and age-matched groups of children. The first group comprised 100 children, aged 6-12 years, with physician-diagnosed persistent asthma with/without other allergic disorders. Two control groups were recruited; the infection group (n=114) included children presenting with acute upper and/or lower respiratory tract infections not necessitating hospital admission and no present or past history suggestive of asthma. The third study group comprised 100 clinically healthy children. Patients having chronic illness other than asthma, or those having significant social, medical or environmental problems unrelated to asthma were excluded from the study.

Ethical Considerations: Informed consent was obtained from the parents before enrollment and after explanation of the aim of the study. The study protocol gained approval of the local Ethics' Committee of the Pediatric Department, Ain Shams University - Cairo, Egypt.

Study Methods:

- Detailed clinical evaluation was conducted including frequency of asthma symptoms, severity, duration, treatment received and adherence to treatment, exacerbations, hospitalization frequency and the presence of other allergic disorders. Physical chest examination was performed at enrollment for the presence of wheeze and signs of respiratory distress. Asthma severity over the past three months and asthma control over the past month were assessed according to GINA.[8]

- Assessment of HRQoL was done by using the EQ-5D-Y questionnaire. The EQ-5D-Y descriptive system comprises the following five dimensions:
    1. *Mobility*
    2. *Looking after myself*
    3. *Doing usual activities*
    4. *Having pain or discomfort*
    5. *Feeling worried, sad or unhappy*
    - Each dimension has three levels: no problems, some problems and a lot of problems. The decision results in a one-digit number that expresses the level of severity selected for that dimension (1 indicates no problems, 2: Some problems and 3: a lot of problems). The digits for the five dimensions can be combined into a five-digit number that describes the patient's health state and is named "health profile". The EQ-5D-Y questionnaire also comprises an additional

visual analogue scale (VAS). It records the patient's self-rated health on a vertical visual analogue scale where the endpoints are labelled "The best health you can imagine"- scored 100 and "The worst health you can imagine"- scored zero. The VAS can be used as a quantitative measure of health outcome that reflects the patient's own judgement.[7]

- Subjects were interviewed in the presence of their parents/caregivers and the questionnaire was interpreted by the same researcher for all subjects.

Statistical methods

Data were analyzed using IBM© SPSS© Statistics version 23 (IBM© Corp., Armonk, NY). Numerical variables were presented as mean and SD and inter-group differences were compared using one-way analysis of variance (ANOVA) with application of the Tukey test for post hoc comparison if needed. Categorical variables were compared using the Pearson chi-squared test or Fisher's exact test when appropriate. Ordinal data were compared using the chi-squared test for trend. Associations between ordinal and continuous variables were tested using the Spearman rank correlation. Rank bi-serial correlation was used to test the association between ordinal and nominal variables. Associations between continuous and nominal variables were tested using point bi-serial correlation. Probability values less than 0.05 were considered significant.

RESULTS

The age and gender distribution of enrolled children are shown in table 1. Among the 100 enrolled asthmatic children, 19% had controlled asthma, 51% had partly controlled asthma and 30% had uncontrolled asthma. According to asthma severity, 58% of patients were categorized as mild to moderate and 42% as severe.

Sixty-four asthmatic children (64%) presented for follow up without having asthma exacerbation. Sixty-Six patients had associated allergic disorders, with allergic rhinitis/rhinosinusitis the most frequently reported (n=56; 56%). Other associated allergies included urticaria/angioedema (9%), allergic rhino conjunctivitis (6%), and eczema (4%). Concerning asthma medications, all cases were on inhaled corticosteroids (ICS) with 24 % on low dose, 70% on medium dose and 6 % on high dose ICS. Systemic corticosteroids (SCS) were received by only 4% while, 58% were on leukotriene receptor antagonists (LTRA). Sixteen patients were receiving regular oral vitamin D therapy. Ninety-two percent of the cases were

adherent to their asthma treatment as reported by their parents.

HRQoL in the asthma group
Dimensions of the EQ-5D-Y questionnaire
The data showed that 86% of the asthma children faced problems with their daily activities (74% of them had some problems and 12% had a lot of problems). Also, 43 patients with asthma suffered from emotional problems in the form of worries, sadness or unhappiness in relation to their illness (31 patients), while 12 had several of these emotional problems (12 patients). Mobility was adversely affected in 22% Thirteen percent of the cases expressed some pain or discomfort due to their disease, while self-care was the least commonly affected among asthmatics (6%). These results are demonstrated in Figure 1.

Associations between the EQ-5D-Y questionnaire dimensions and asthma patients' characteristics (Tables 2 and 3)
Mobility problems were positively associated with age, disease duration, asthma control and use of inhaled long acting beta-2 agonists (LABA) as well as moderate positive association with the VAS score results. The dimension of *doing usual activities* showed a strong positive association with VAS score and moderate positive association with the degree of asthma control, but weak positive association with the asthma disease duration, and intake of SCS and its dose, leukotriene receptor antagonist (LTRA) and LABA. The parameter of *having pain or discomfort* showed a strong positive association with the VAS scores, but the association was weak with age, intake of SCS and its dose and asthma control. *Feeling worried, sad or unhappy* showed strong positive association with the VAS scores but was moderately associated with age, asthma duration and control. Weak positive associations were found in relation to asthma exacerbations and LABA use, and inverse association with adherence to asthma treatment. The VAS scores correlated negatively to age, frequency of asthma exacerbations, or SCS dose, LABA use, asthma duration and level of asthma control.

Comparison between the study groups
EQ-5D-Y dimensions: Parameters of *mobility, doing usual activities, feeling worried or sad* were more frequently impacted among the asthmatic children in comparison to the other two groups (X^2 = 37.02, 46.38, and 22.89, respectively; p <0.001). On the other hand, the parameter of *having pain or discomfort* was most commonly affected among the infections' group in comparison to the other two groups. The parameter of *looking after myself* was comparable among the three studied groups (Table 4).
VAS score: Asthmatic patients had the lowest VAS scores (range: 10-100; mean± SD: 72.2 ± 24.6) in comparison to the infection and healthy control groups (mean± SD: 84.6 ± 12.2 and 92.8 ± 9.6, respectively; f=39.03, p- value = 0.001.

Health profiles
We outlined 32 different health profiles in this study. The three study groups varied significantly in their health profiles according to the EQ-5D-Y questionnaire (p<0.001). Among asthmatics, there were 22 different health profiles, most common (39%) of which was 11211 (some problems in doing usual activities), followed by 11212 in 17% of patients (some problems in the activities and emotionally). The most common reported health profile in the infection group was 11221 (some problems with doing usual activities and having pain or discomfort) being expressed in about 51% of patients. The health profile 11111 (no problems in all five dimensions of the questionnaire) was expressed in 27% of healthy control, 13% of asthmatics and 3.5% of the infection group. In the healthy control group, 11111 (no problems in all dimensions of the questionnaire) was the most commonly detected health profile (27%) (Figure 2).

Table 1. Demographic characteristics of the three study groups

Variable	Bronchial Asthma (n=100)	Infections (n=114)	Healthy Control (n=100)	F	p value*
Age (years)	8.3 ± 2.1	8.3 ± 1.8	8.2 ± 1.9	2,311	0.815*
Gender (F/M)	38/62	54/60	48/52	-0.204	0.285#

Data are mean ± SD or ratio; *One-way analysis of variance (ANOVA); #Fisher's exact test.

Table 2. Correlation between different EQ-5D-Y dimensions and other variables in asthmatic children

Variable	Correlation	EQ-5D-Y Dimension					
		Mobility	Looking after myself	Doing usual activities	Having pain or discomfort	Feeling worried, sad or unhappy	VAS score
Age	Coefficient	.323**	.164	.067	.207*	.418**	-.348**
	P-value	.001	.103	.507	.039	<.001	<.001
Gender	Coefficient	.068	-.149	.051	.058	.075	-.062
	P-value	.504	.138	.614	.569	.456	.539
Disease duration	Coefficient	.205*	-.102	.274**	.144	.424**	-.421**
	P-value	.041	.314	.006	.154	<.001	<.001
Exacerbations	Coefficient	.205*	.104	.070	.072	.339**	-.267**
	P-value	.040	.302	.490	.479	.001	.007
Associated allergies	Coefficient	-.150	.251*	.052	-.080	.059	-.039
	P-value	.136	.012	.607	.431	.557	.702
Asthma severity	Coefficient	.043	-.125	.057	.155	.007	-.001
	P-value	.673	.217	.575	.124	.944	.995
Asthma control	Coefficient	.339**	.021	.537**	.291**	.450**	-.542**
	P-value	.001	.837	<.001	.003	<.001	<.001

*. Correlation is significant at the 0.05 level (2-tailed).
**. Correlation is significant at the 0.01 level (2-tailed).

Table 3. Correlation between different EQ-5D-Y dimensions and medications, compliance and VAS score in asthmatic children

| Variable | Correlation | EQ-5D-Y Dimension | | | | | VAS score |
		Mobility	Looking after myself	Doing usual activities	Having pain or discomfort	Feeling worried, sad or unhappy	
Systemic steroids	Coefficient	.138	-.052	.207*	.225*	.047	-.129
	P-value	.171	.610	.039	.025	.643	.200
Prednisone dose	Coefficient	.143	-.052	.207*	.231*	.048	-.130
	P-value	.156	.610	.039	.021	.634	.199
Inhaled steroids	Coefficient	.022	.151	-.069	.055	-.121	.062
	P-value	.829	.134	.494	.585	.230	.543
LTRA	Coefficient	.012	-.126	.206*	.088	.194	-.157
	P-value	.908	.211	.039	.384	.053	.118
LABA	Coefficient	.278**	-.021	.264**	.030	.373**	-.207*
	P-value	.005	.835	.008	.769	<.001	.039
Vitamin D	Coefficient	.163	.119	-.036	-.006	.124	-.039
	P-value	.105	.237	.725	.949	.218	.702
Compliance	Coefficient	-.199*	-.236*	-.155	-.105	-.226*	.174
	P-value	.047	.018	.125	.297	.024	.083
VAS score	Coefficient	-.452**	-.323**	-.641**	-.419**	-.860**	
	P-value	<.001	.001	<.001	<.001	<.001	

*. Correlation is significant at the 0.05 level (2-tailed).
**. Correlation is significant at the 0.01 level (2-tailed).

Table 4. Results of EQ-5D-Y questionnaire in the three studied groups

EQ-5D-Y dimension	Parameter affection	Bronchial Asthma (n=100)		Infection group (n=114)		Healthy controls (n=100)		$\chi^2(1)$	p-value*
		n	%	n	%	n	%		
Mobility	No problems	78	78.0%	114	100.0%	100	100.0%	37.024	<0.001
	Some problems	22	22.0%	0	0.0%	0	0.0%		
	A lot of problems	0	0.0%	0	0.0%	0	0.0%		
Looking after myself	No problems	94	94.0%	104	91.2%	100	100.0%	3.710	0.054
	Some problems	6	6.0%	10	8.8%	0	0.0%		
	A lot of problems	0	0.0%	0	0.0%	0	0.0%		
Doing usual activities	No problems	14	14.0%	14	12.3%	52	52.0%	46.379	<0.001
	Some problems	74	74.0%	95	83.3%	48	48.0%		
	A lot of problems	12	12.0%	5	4.4%	0	0.0%		
Having pain or discomfort	No problems	87	87.0%	21	18.4%	49	49.0%	22.897	<0.001
	Some problems	13	13.0%	81	71.1%	50	50.0%		
	A lot of problems	0	0.0%	12	10.5%	1	1.0%		
Feeling worried, sad or unhappy	No problems	57	57.0%	106	93.0%	100	100.0%	61.518	<0.001
	Some problems	31	31.0%	7	6.1%	0	0.0%		
	A lot of problems	12	12.0%	1	.9%	0	0.0%		

Data are number (n) and percentage (%); χ^2 = chi-squared statistic; *Chi-squared test for trend.
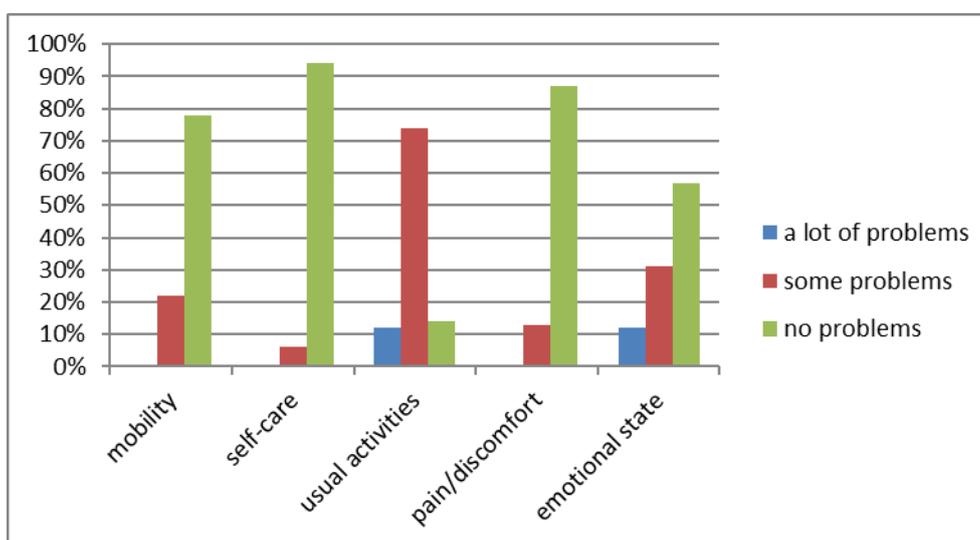

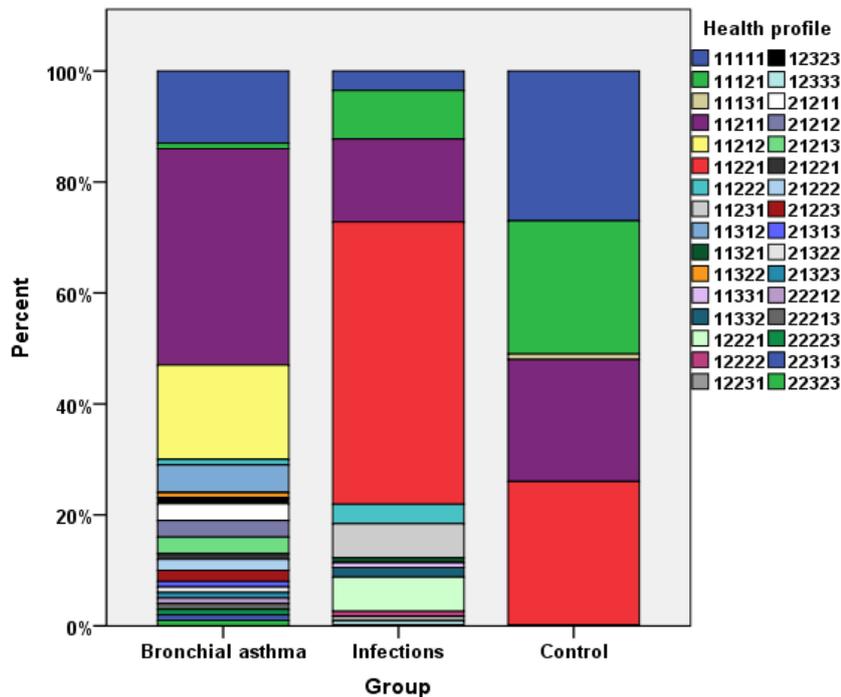**Figure 1.** EQ-5D-Y dimensions among the studied asthmatic children.

Figure 2. Health profiles according to the EQ-5D-Y questionnaire among the three study groups.

DISCUSSION

We applied a HRQoL questionnaire on a group of asthmatic Egyptian children aiming to investigate the real impact of asthma on their quality of life. HRQoL was estimated among the asthmatic Egyptian children before but none of the studies used the EQ-5D-Y questionnaire.[10-13]

Healthy children might have their quality of life affected owing to several factors including multidimensional poverty, crowdedness and multiple deprivations related to lack of access to services and support mechanisms. It is estimated that 28% of Egyptians are living below the national monetary poverty line.[14] We enrolled children from a university hospital that offers medical care for economically unprivileged patients. A group of children with respiratory tract infections was included as a second control group as infection is quite prevalent in Egyptian children whether asthmatic or not especially in the context of malnutrition and poor living conditions.[15-17]

The three groups enrolled were quite matched in terms of age, gender and socioeconomic status. The study revealed that HRQoL is adversely affected in the asthmatic group; this was noticeable from their health profiles and VAS scores. It involved all aspects of children's lives namely social, mental, physical and emotional. Our findings are consistent with many previous studies that investigated and

discussed the impact of asthma on HRQoL and reported significant adverse effects.[9,18,19]

The most affected aspect in the asthmatic group in our series was the physical function with problems in the "doing usual activities" dimension. The asthmatic children stated that the main issue with activity limitation was in their school absenteeism affecting their scholastic achievement, in addition to the impact on their playing with peers and doing sports. The ability to do their daily routine tasks with their families was also impaired. This item of the questionnaire showed significant positive association with the asthma duration, asthma control and VAS score. Furthermore, it correlated significantly with the need of add-on controllers (LTRA and LABA) and the required systemic corticosteroid dose to control symptoms. Noteworthy, only 19% of our series had controlled asthma while 51% had partly controlled and 30% had uncontrolled asthma.

In agreement with our findings, a study on Brazilian children and adolescents with asthma (7-17 years old) revealed that the *activity limitation domain* was lowest in comparison to other domains of the Pediatric Asthma Quality of Life Questionnaire (PAQLQ); this was more obvious in the children with poorest asthma control and greatest asthma severity.[20] Similar findings were reported as well by Josie et al. in disadvantaged

African American youth.[21] EQ-5D-Y performed better than other generic questionnaires such as PedsQL 4.0 which was not sensitive enough to distinguish HRQoL between children with different levels of asthma severity and control in relation physical activity.[22]

Mobility also was adversely affected among our series as 22% had some problems walking around. The main influencing factors on this dimension were age, disease duration and asthma control. Poor asthma control limits the mobility of asthmatic children. In addition, increased disease duration might be associated with more structural airway changes, further limiting the ability to walk about.[23] Reimberg and colleagues[24] noted that asthmatic children and adolescents who need regular asthma treatment have reduced functional capacity and exhibit a sedentary behavior.

The dimension of *feeling worried, sad or unhappy* was the second most affected parameter of HRQoL in our asthmatic group as 31% of children reported some problems within this dimension and 12% suffered a lot of problems. Interviewed children attributed that feeling to their fears of having exacerbations in an inappropriate place or in front of their friends. Bergfors et al [9] studied 94 Swedish children with asthma, aged 8 to 16 years. They used the EQ-5D-Y and the pediatric asthma quality of life (PAQLQ) questionnaires and found that, emotional and mental aspects were significantly affected. In the same context, Shankar et al.[25] used the Center for Epidemiological Studies Depression Scale and found that 28% of 277 urban asthmatic adolescents had depressive symptoms that were associated with less sleep and impaired physical activity. In a relevant study, a generalized anxiety disorder and emotional dependency of asthmatic children on their care givers were observed.[26] These observations collectively show the importance of psychological support to patients and caregivers in the context of asthma management.

We demonstrated that the emotional status of asthmatic children is significantly influenced by age, asthma duration, presence of exacerbation and poor asthma control. As children grow-up, they become emotional and stressed due to pubertal changes and their disease perception especially when they have partial or poor asthma control.[27,28] In a study that comprised 140 Egyptian asthmatic children, the authors noted that poor access to medications was one of the factors that adversely affected the patient PAQLQ scores.[11] On the other hand, having emotional problems reduces the patients' adherence to treatment leading to reduced level of asthma control.[29,30]

Having pain or discomfort was affected in only 13% of our asthma patients. The affection of this dimension is expected to occur with acute rather than chronic medical illnesses during asthma exacerbations and may be linked to poor asthma control.[31] The dimension named *looking after myself* was the least affected one among the studied asthmatic patients with some problems only in 6%. Impaired self-care would be expected during acute severe asthma exacerbation with marked compromise of respiratory functions while our series comprised outpatients. This dimension was associated with the presence of other concomitant allergies which might compromise their ability to self-administer excessive medications.

Asthma control but not asthma severity had significant impact on the results of the EQ-5D-Y questionnaire as far as several parameters were concerned including mobility, doing usual activities, having pain or discomfort, and feeling worried, sad or unhappy as well as the VAS score. Asthma control is probably the most valuable determinant of HRQoL whatever the level of disease severity is.[32-34]

Nevertheless, a proportion of our asthmatic children (13%) reported no problems in all the 5 dimensions. This was previously reported by Bergfors et al who used the PAQLQ in addition to the EQ-5D-Y and found that 50% of their asthma children had a health profile of 11111 denoting no problem.[9] This observation was considered by some investigators to reflect a ceiling effect which means that the EQ-5D-Y might not be able to operate when the participant's status is close to full health.[35,36]

Expectedly, the most frequent reported health profile in our asthma patients was 11211 that points to having some problems in doing usual activities. Among the infection group participants, the health profile 11111 represented only 3.5%, while the most commonly reported profile was 11221 (having pain and discomfort and difficulty in doing usual activities). The observation reflects the ability of the EQ-5D-Y questionnaire to reflect acute health problems including acute infections making them feel pain or discomfort.

In conclusion, our results indicate that bronchial asthma has a significant adverse impact on HRQoL of children and that EQ-5D-Y questionnaire could be a valuable instrument to assess it. The asthmatic children had impaired parameters of doing usual activities, having pain or discomfort, and feeling worried, sad or unhappy, as well as limited

mobility. The findings are indeed limited by the sample size and cross-sectional study design. The consecutive manner of enrollment hindered the distribution of the sample according to severity and level of control. We recommend the integration of asthma related QoL assessment and psychosocial screening to the routine pediatric asthma care to improve the well being of the children. Prospective wider-scale studies are needed to confirm our conclusions. Translation and validation of the EQ-5D-Y questionnaire into the Arabic language is also needed to be more feasible and to decrease bias during the interpretation of the results.

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