INTRODUCTION

Asthma is a heterogeneous chronic inflammatory disease, characterized by recurrent episodes of wheezing, dyspnea, chest tightness, and cough, that is common in children and adolescents ***(de Benedictis and Attanasi, 2016).***

Optimal asthma management aims to maintain the usual daily activities, decrease asthma exacerbations, keep normal lung function with prevention of treatment side effects ***(Lozier et al., 2019).***

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 ***(La Scala et al., 2005).***

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 routine and the quality of life of all involved family members ***(Stelmach et al., 2012).*** Thus, it is necessary to characterize quality of life in children and adolescents with asthma treated at asthma referral centers.

The understanding of the extent to which asthma control status and asthma severity can affect quality of life will help establish therapeutic, environmental, and behavioral strategies, resulting in increased awareness within the health care system, so that interventions allowing a favorable disease outcome are promoted ***(Matsunaga et al., 2015).***

Different questionnaires have been developed to assess health related quality of life (HRQoL). EQ-5D-Y is a newly developed generic instrument, based on the EQ-5D adult version, which provides the opportunity to address a child's HRQoL, regardless of the disease ***(Ravens-Sieberer et al., 2010).***

The EQ-5D-Y instrument consists of a descriptive system with five dimensions: 'mobility', 'looking after myself', 'doing usual activities', 'having pain or discomfort' and 'feeling worried, sad or unhappy'. It also features an additional visual analogue scale (VAS) on the current health state ***(Wille et al., 2010).***

Aim of the Study

The aim of this study is to assess the feasibility and convergent validity of the EQ5D-Y instrument in Egyptian children with asthma. In addition, we sought to measure the health-related quality of life (HRQoL) of asthmatic children in relation to their asthma severity and control, using the EQ-5D-Y questionnaire, in comparison to a group of matched controls. The ultimate objective is to alleviate morbidity in these children and help them lead a normal life.

QUALITY OF LIFE

Historically, studies of patient outcomes in asthma have focused on clinical and physiologic measures. More recently, however, there is growing recognition that such clinical measures do not provide a complete, or in some cases, accurate, view of the impact of a disease on an individual's physical, social, or emotional well-being ***(Nalina et al., 2015).***

The last decade has seen a shift in the management of asthma in clinical practice. Rather than managing patients based on their severity, current clinical practice guidelines emphasize that the overall goal of management is to achieve symptom control. Good asthma control has been shown to be associated with improved health status ***(Dean et al., 2010).***

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Measuring HRQoL is one approach to assess how children and adolescents perceive their health. HRQoL is a concept that

covers an individual's well-being in relation to the physical, emotional and social aspects of their health ***(Rutishauser et al., 1998).***

HRQoL is affected in a complex way by the persons' physical health, psychological state, level of independence, social relationships, personal beliefs, and their relationships to salient features of the environment. The HRQoL of children with asthma is adversely affected by disease-specific parameters, such as asthma severity and poor asthma control ***(Kalyva et al., 2016).***

Children and adolescents with asthma often feel unhealthy or feel that they do not have the same opportunities as their peers when it comes to physical activities. Many aspects of their lives are affected. As well as suffering symptoms, and being limited in their physical activities, they also suffer from the fear of having an asthma attack, and some children are bullied ***(Bergfors et al., 2015).***

Health-related quality of life has been considered an important variable to be managed in airway diseases. Asthma can reduce HRQoL as a result of profound physical and psychosocial complications. Besides physical symptoms, asthma patients may exhibit fatigue, psychomotor sluggishness, irritability and mood and cognitive disturbances. This combination of physical, emotional, and functional problems may diminish HRQoL ***(Nalina et al., 2015).***

In developing countries, chronic respiratory diseases represent a challenge to public health because of their increasing frequency and severity and the projected trends and economic impact. It is estimated that asthma accounts for about 2,50,000 deaths per year worldwide ***(Nalina et al., 2015).***

Measures of HRQoL in asthmatic children:

Quality of life measures provide information on how chronic diseases influence social, emotional, and physical aspects of life from patient's perspective. HRQoL evaluation is performed by using questionnaires that can be generic or specific. Generic questionnaires address HRQoL in general, whilst specific questionnaires address the impact of certain diseases on QoL ***(Fayers, 2007).***

Disease-specific tools of QOL are more responsive and clinically useful than generic QOL tools which focus on nonspecific general condition, while generic measures are good at comparisons of QOL burden and medications benefit across diseases. Disease-specific measures are characterized by specificity through measuring the frequency and severity of specific symptoms. Disease-specific and generic tools have a complimentary relationship. For instance, generic measures can monitor changes in the physical functioning of patients over time in relation to population norms, regardless of the cause of any change. Disease-specific measures can help determine which

conditions accounted most for a patient's limitations in physical functioning ***(Ware et al., 2016).***

There are many specific questionnaires to evaluate HRQoL of asthmatic children. The most frequently used are pediatric asthma quality of life questionnaire (PAQLQ), pediatric quality of life inventory 4.0 (PedsQL-Asthma), and disability kids (DISABKIDS), these three tools more practical and have adequate psychometric characteristics ***(Roncada et al., 2013).***

The next questionnaires are the most frequently used ones in evaluation of HRQoL of asthmatic children and adolescents:

The Pediatric Asthma Quality of Life Questionnaire (PAQLQ):

PAQLQ is a disease-specific questionnaire for asthmatic children. It is innovated to assess QoL in children aged from 7 to 17 years old. The PAQLQ was developed and validated by ***Juniper et al. (1996).***

The PAQLQ is an evaluative instrument that is highly sensitive to tiny changes over time, within the patient and therefore is optimum for capturing the effect of an intervention in a clinical trial. PAQLQ has been validated and applied to the assessment of the QoL of asthmatic children in the USA, Europe and some Asian countries ***(Poachanukoon et al., 2006).***

PAQLQ includes 23 items in three domains (activity limitation, symptoms and emotional functions). The activity limitation domain included five items relating to play, sports and

other activities. Ten items are covered in the symptoms' domain including cough, wheezing and nocturnal awakening. The emotional function domain contained eight items such as being frightened, frustrated, irritable or worried, etc. Response to each item ranged from 1 (maximum impairment) to 7 (no impairment at all) ***(Juniper et al., 1996).***

PAQLQ is designed for evaluative purposes due to its responsiveness to change over time, but it is also a good discriminative tool, due to its ability to differentiate between cases with better and cases with worse quality of life. A major obstacle with the PAQLQ is that a single version covers the age range 7–17 years. On the other hand, this wide age range may allow broad comparisons between different age groups (Table 1) ***(Rutishauser et al., 1998).***

Pediatric Quality of Life Inventory 4.0 (PedsQL):

This is a generic tool, that was designed to measure HRQoL in children and adolescents aged 2 -18 years. It has 23 items divided into five domains: physical functional status, emotional functional status, social functional status, and school functional status. The fifth domain is the psychosocial, consisting of the sum of the domains, except for the physical. There are versions self-administered from 5 years of age, and it also has versions that can be answered by proxy. PedsQL 4.0 was designed to be used independently or together with modules separated from the questionnaire and designed for specific diseases, including asthma.

PedsQL3.0-Asthma (asthma module) has 28 multidimensional items that assess asthma symptoms, treatment problems, concerns and communication ***(Varni et al., 2004).***

Table (1): PAQLQ questionnaire

Scores	Aspects
LIMITED ACTIVITY	
1	Strong physical activity
2	Medium physical activity
3	Social activity
4	Work-related activities
5	Sleepiness
SYMPTOMS	
8	Shortness of breath
14	Dull aching chest
18	Expiratory or inspiratory difficulties, early morning symptoms of asthma
24	Night arousal
ENVIRONMENT	
9	Smoke,
17	Dust
23	Air pollution environment
26	Strong smell symptoms,
25	Air pollution of the environment
28	Strong smell had to be avoided
EMOTION	
6	Chest tightness caused by the degree of discomfort
7	Worried about suffering from asthma
12	Cough caused by discomfort
13	Asthma and worry
15	Medication
16	Clear throat
21	Worry about no asthma medication
22	Heavy breathing
27	Fear of breathlessness
29	Remuneration,
30	Desperately breathing,
10	Limitation of conscious activities

PAQLQ: Pediatric Quality of Life Inventory 4.0

(Wang et al., 2018)

DISABKIDS:

The DISABKIDS Chronic Generic Module (DCGM-37) is a questionnaire which measures general HRQoL and the level of affection caused by a chronic disease, and can be supplemented with condition-specific modules for asthma and some other chronic diseases like arthritis, cerebral palsy, cystic fibrosis, dermatitis, epilepsy and diabetes. The instrument includes two forms, one filled by children aged from 8 - 18 years, and the second filled by their parents with four-weeks recall period for all items ***(Roncada et al., 2013).***

The DISABKIDS asthma module consists of 11 items and two domains: the impact domain (six items) relating to restrictions and symptoms, and the concerns domain (five items), about fears related to asthma ***(Roncada et al., 2013).***

The DCGM-37 questionnaire contains 37 items which explore six dimensions of HRQoL (Figure 1). "Mental independence" evaluates whether the child feels confident about the future and is able to lead a normal life without impairments caused by his disease, "Mental emotion" assesses emotional reactions, such as worries, concerns and problems caused by the child's disease, "Social exclusion" it is about feeling of being stigmatized, "Social inclusion" concentrated on positive social relationships and the understanding of others, "Physical limitation" refers to somatic limitations, caused by the disease and "Physical treatment" evaluates the effect of taking medications. Each item's

score indicates the frequency of behaviors, as 1 = never, 2 = seldom, 3 = quite often, 4 = very often, 5 = always. From the row score a total score computed with a range from 0 to 100 with higher scores indicating higher self-perceived HRQoL ***(Frøisland et al., 2012).***

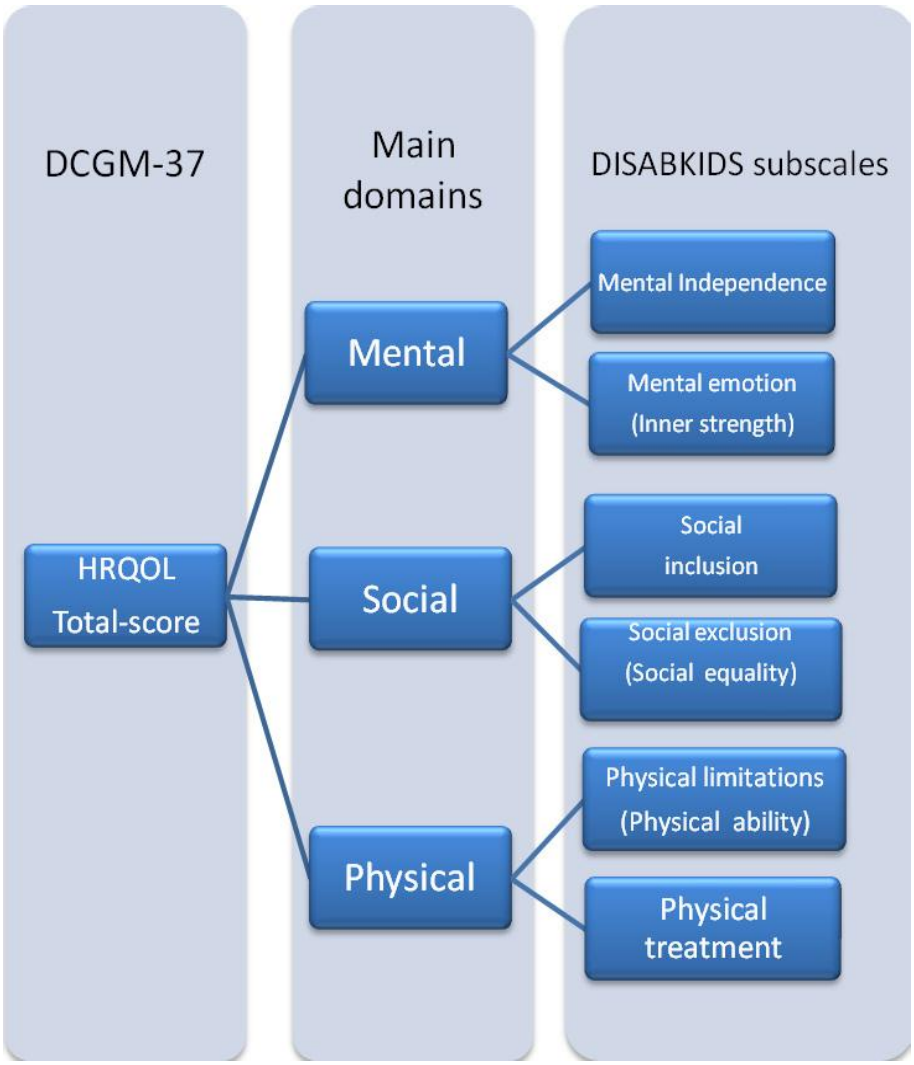

Figure (1): The structure of the DISABKIDS Chronic Generic Module-37, (DCGM-37), included rephrased, positive subscales, (in parenthesis) ***(Roncada et al., 2013)***

Adolescent Asthma Quality of Life Questionnaire (AAQOL):

AAQOL developed in Australia in 2001 to measure the HRQoL of adolescents with asthma (12-17 years old). It is a multidimensional, self-administered questionnaire that estimates the impact of asthma on the physical, emotional, and social aspects of asthmatics' life. The final version consists of 32 items divided into five domains: symptoms, medications, physical activity, emotions, and social interaction. There is also a sixth domain (positive effects) that does not count in the total score of the tool, but provides complementary information ***(Rutishauser et al., 2001).***

About My Asthma (AMA)

It is used to assess the stress that affect asthmatic children and adolescents' HRQoL with age between 6 -12 years. The AMA is a self-administered questionnaire. It has 55 items, with which participants can classify their thoughts and feelings in a four-point scale. The total score represents asthma stressors intensity, the score ranges from 1 to 55 points ***(Mishoe et al., 1998).***

Asthma Symptoms and Disability Questionnaire (ASDQ)

The questionnaire is designed to evaluate HRQoL of children and adolescents aged 5 to 14 years. The ASDQ is a proxy questionnaire, answered by caregivers or adolescents. The final version contains17 items divided into three domains: disability, daytime symptoms, and nighttime symptoms ***(Usherwood et al., 1990).***

Pediatric Asthma Health Outcome Measure (PAHOM)

A tool developed to assess HRQoL in children with asthma, aged 5 to 12 years. It has71 items divided into seven dimensions: absence of Respiratory symptoms, moderate respiratory problems, severe respiratory problems, no emotional problems, presence of emotional problems, lack of activity problems, and presence of activity problems. This questionnaire includes a calendar as a visual aid to help the children remember their health condition a week before ***(Chiou et al., 2005).***

How Are You (HAY)

This questionnaire is used to evaluate the HRQoL of asthmatic children aged 8 to 12 years. HAY is self-administered and proxy at the same time. It contains three dimensions: physical activities, social activities, and self-management. The questionnaire consists of generic and specific sections for asthma, the generic section can be answered either by asthmatic or healthy children and includes (physical activity, cognitive activities, social activities, and physical complaints) domains. Regarding the specific section, it consists of: (symptoms of asthma, self-management, asthma-related emotions, and self-concept) domains ***(Coq et al., 2000).***

Kinder Lebensqualitat Fragebogen (KINDL-R)

A generic instrument designed in to evaluate HRQoL of children and adolescents. It is a self and proxy administered questionnaire, that has three versions: Kiddy-Kindl (4 -7 years old), Kid-Kindl (8 -11 years old), and Kiddo-Kindl (12 -16 years old). In

addition to the generic versions, the KINDLR has six modules to evaluate quality of life of children with specific diseases: asthma, diabetes, epilepsy, neurodermatitis, oncology, and spina bifida. The generic KINDL-R version contains 24 items, divided on six dimensions: physical and emotional well-being, self-esteem, family, friends, and daily usual activities. The subscales of these six dimensions are combined to produce a total score. The asthma module of this questionnaire has 15 items ***(Roncada et al., 2013).***

Childhood Asthma Questionnaires (CAQ)

This questionnaire has been developed to assess HRQoL and the level of stress the disease causes. The tool consists of three versions, depending on the age of the subjects: CAQ-A for children 4 to 7 years; CAQ-B for 8 to 11 years; and CAQ-C for 12 to 16 years ***(Roncada et al., 2013).***

Roncada et al. (2013) summarized some important HRQoL measures and their characteristics in tables 2 and 3.

Table (2): General characteristics of specific instruments to assess quality of life in children and adolescents with asthma

Tool	Items	Domains (n)	Domains	Age (years)	Respondent	Country of origin	Year of validation	Validated in Brazilian Portuguese
AAQOL	32	6	Symptoms, medications, physical activity, social interaction, and emotions	12-17	Adolescents	Australia	2001	No
KINDL-R	15	6	Physical well-being, emotional well-being, self-esteem, family, friends, and daily functional activity	4-7 8-11 12-1	Parent/tutor Children Adolescents	Germany	2000	No
PAQLQ	23	3	Symptoms, emotions, and activity limitations	7-17	Children	Canada	1996	No
LAQCA	71	7	Physical activities, work activities, outdoor activities, emotions and emotional behaviors, homecare, eating and drinking, others	5-17	Children	USA	1993	Yes
AMA	55	1	Thoughts and feelings	6-12	Children	USA	1998	No
ITG-CASF	17	3	Daytime symptoms, nighttime symptoms, and functional limitations	2-17	Parent/tutor	USA	2004	No
PedsQL	28	4	Symptoms of asthma, problems with treatment, concerns, and communication	2-18	Children	USA	2004	No
PAHOM	7	3	Symptoms, emotions, and activities	7-12	Children	USA	2005	No
DISABKIDS	11	2	Impact and concerns	8-16	Children	Europe	2005	No
HAY	38 and 40	6	Physical activity, cognitive activity, social activity, physical complaint, emotions related to asthma, asthma symptoms, self-esteem, and self-management	8-12	Children	the Netherlands	2000	No
TACQOL	34	5	Complaints, situations, treatment, medication, and emotions	8-16	Children	the Netherlands	2006	No
ASDQ	17	3	Disabilities, daytime symptoms, and nighttime symptoms	5-14	Parent/tutor	England	1990	No
CAQ	CAQ-A: 14 CAQ-B: 23 CAQ-C: 46	2 4 5	Quality of life (active and adolescence), anxiety, severity, and reactivity	4-7 8-11 12-16	Children Children Adolescents	England	1993	No
JSCA-QOL v3	25	5	Asthma symptoms, changes in daily life, family support, daily life satisfaction, and restriction in participation in daily activities	10-18	Children	Japan	2006	No
ARQOL	35	4	Restriction in social activities, physical disorders, limitations in physical activity, inconvenience in the daily management of the disease, and emotional distress	7-1	Children	Taiwan	2006	No

*Developed and validated in cooperation with the following countries: Austria, France, Germany, Greece, the Netherlands, Sweden, and England.
AAQOL, Adolescent Asthma Quality of Life Questionnaire; AMA, About My Asthma; ARQOL, Asthma Related Quality of Life; ASDQ, Asthma Symptoms and Disability Questionnaire; CAQ, Childhood Asthma Questionnaires; DISABKIDS, Disability Kids; HAY, How Are You; ITG-CASF, Integrated Therapeutics Group Child Asthma Short Form; KINDL-R, Kinder Lebensqualität Fragebogen; LAQCA, Life Activities Questionnaire for Childhood Asthma; PAHOM, Pediatric Asthma Health Outcome Measure; PAQLQ, Paediatric Asthma Quality of Life Questionnaire; PedsQL, Pediatric Quality of Life Inventory 4.0; JSCA-QOL, Quality of Life Questionnaire for Japanese School-aged Children with Asthma; TACQOL-Asthma, TNO-AZL Questionnaires for Children's Health-Related Quality of Life.

(Roncada et al., 2013)

Table (3): Characteristics of validation and publication of specific tools to assess quality of life in children and adolescents with asthma

Tool	Patients included	Validity	Internal consistency	Sensitivity to change	Test/retest	Year of validation	Validation in Brazilian Portuguese	Articles published[a]	Mean number of articles published per year
AAQOL	111	+	αC	+	+	2001	No	9	0.81
KINDL-R	254	+	αC	+	+	2000	No	39	0.75
PAQLQ	52	+	-	+	+	1996	Yes	57	3.56
LAQCA	92	+	αC	-	+	1993	No	1	0.05
AMA	35	+	αC	+	+	1998	No	1	0.07
ITG-CASF	181	+	αC	+	-	2004	No	6	0.75
PedsQL	401	+	αC	+	+	2004	No	22	2.75
PAHOM	72	+	-	-	-	2005	No	1	0.14
DISABKIDS	1,094[b]	+	αC	-	-	2005	No	12	1.71
HAY	80	+	αC	+	+	2000	No	2	0.16
TACQOL	298	+	αC	+	+	2006	No	3	0.50
ASDQ	52	+	αC	+	+	1990	No	1	0.04
CAQ	242	+	αC	+	+	1993	No	5	0.26
JSCA-QOL v3	2,425	+	αC	+	+	2006	No	1	0.16
ARQOL	474	+	αC	+	-	2006	No	2	0.33

AAQOL, Adolescent Asthma Quality of Life Questionnaire; AMA, About My Asthma; ARQOL, Asthma Related Quality of Life; ASDQ, Asthma Symptoms and Disability Questionnaire; CAQ, Childhood Asthma Questionnaires; DISABKIDS, Disability Kids; HAY, How Are You; ITG-CASF, Integrated Therapeutics Group Child Asthma Short Form; KINDL-R, Kinder Lebensqualität Fragebogen; LAQCA, Life Activities Questionnaire for Childhood Asthma; PAHOM, Pediatric Asthma Health Outcome Measure; PAQLQ, Paediatric Asthma Quality of Life Questionnaire; PedsQL, Pediatric Quality of Life Inventory 4.0; JSCA-QOL, Quality of Life Questionnaire for Japanese School-aged Children with Asthma; TACQOL-Asthma, TNO-AZL Questionnaires for Children's Health-Related Quality of Life; αC, Cronbach's alpha coefficient.

[a] PubMed, Ovid, and LILACS, 15 tools from nine countries.

[b] Developed and validated in cooperation with the following countries: Austria, France, Germany, Greece, the Netherlands, Sweden and England.

(Roncada et al., 2013)