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Health-Related Quality of Life in School Children with Short Stature in Gharbia Governorate in Egypt

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ABSTRACT
Background: Short stature (SS) in a child is defined as a child 2 or more standard deviations below the mean height for children of that gender and chronological age**.** Health-related quality of life (HRQOL) reflects physical, psychological, social, cognitive, functional and behavioral dimensions of well-being and functioning as perceived by the person concerned, in a wide range of conditions between excellent and poor health.
Objective: To assess HRQOL for children and adolescents with short stature (SS).
Patients and Methods: In order to assess the HRQOL for SS patients, we studied 392 school children (preparatory and secondary) who meet the diagnosis of SS according to definition of WHO for short stature of child height below or equal 3rd percentile on WHO Growth chart in children of same gender and chronological age . Both sexes were included and age ranged from 12 to 18 years.
Results: According to family history, more than 2/3 of the children with SS had negative consanguinity. 1.5% was with positive family history of a similar condition and 15 % had positive family history of chronic disease. There was significant lower HRQOL in children with SS concerning physical, psychological and environmental World Health Organization Quality of Life (WHOQOL) domains. The psychological domain is the most affected one. A comparison of sex groups (males and females) in relation to different domains among cases but it did not reach statistically significant difference.
Conclusion: Pediatric patients with SS have lower HRQOL. Social domain is the most affected among SS children.
Keywords: Short stature, Health-related quality of life, Gharbia Governorate.

INTRODUCTION

Short stature (SS) in a child is defined as a child 2 or more standard deviations below the mean height for children of that gender and chronological age**.** A child's growth is important because it is a strong indicator of his or her health. SS in a child must be fully investigated to distinguish between a normal variation and an underlying pathological condition [(1)]**.** Short stature in children may have different causes, including normal variation, genetic defects, malnutrition, chronic systemic disease, endocrine disorders or psychosocial deprivation. Growth hormone deficiency (GHD) represents a relatively rare cause for SS, which is due to insufficient secretion of growth hormone [(2)]**.**

Among children without GHD, short stature may be caused by Turner syndrome, chronic renal insufficiency, being small for gestational age at birth, Prader-Willi syndrome, or other conditions. When the cause is unknown, it is called idiopathic SS [(3)]**.**

The child's history is an important step for evaluation of SS. Whenever possible, obtain the original birth records to document length, weight and skull circumference at birth to exclude intrauterine growth retardation, also the mode of delivery to exclude abnormal presentation or difficult and traumatic delivery. The medical history should also include the presence of other members of the family with a similar condition to exclude a genetic cause, familial SS or constitutional delay of growth and development [(4)]**.**

HRQOL reflects physical, psychological, social, cognitive, functional and behavioral dimensions of well-being and functioning as perceived by the person concerned, in a wide range of conditions between excellent and poor health. The concept of HRQOL is therefore increasingly considered as a relevant 'patient-reported outcome [(5)]**.** As a multidimensional construct, HRQOL offers the possibility to focus on different aspects of well-being and functioning and addresses the subjective perceptions of individuals. HRQOL evaluation of SS broadens our understanding of the psychosocial impact of this condition, by providing insights into potential impairments of functioning and well-being in comparison to other clinical and non-clinical populations. In addition, the effects of treatment in patient cohorts can serve as an empirical basis for clinical decision making as well as individual tailoring of treatment [(6)]**.**
The present work aimed to assess health-related quality of life (HRQOL) for children and adolescents with short stature (SS).

PATIENTS AND METHODS

Cross-sectional study that was conducted in Gharbia Governorate on preparatory and secondary school children.

Inclusion criteria: School children who meet the diagnosis of SS according to the definition of WHO for short stature of child height below or equal 3rd

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percentile on WHO Growth chart in children of same gender and chronological age. Both sexes were included with age from 12 to 18 years.

Exclusion criteria: Children with any other chronic diseases, dysmorphic appearance or disabilities that affect their quality of life

Sample size: Assuming that total number of preparatory and secondary school children was 125000 and prevalence of short stature was 15% sample was calculated to be 196 children using EPI Info 7 program with test power 80% CI (Confidence Interval) 95% sample size was 196 multiblied by 2. So the sample size was 392.

Methods:

Evaluation of a child with short stature:

A. History taking: Age, name, sex, socio-demographic variables (residence, occupation and education level of patient's father and mother), age at time of diagnosis, history of factors that could compromise the QOL, complications or associated conditions and exercise. Family history included consanguinity, same short stature cases in the family and history of chronic diseases.

B. Examination: To exclude dysmorphic appearance or disabilitis, any chronic illness that affects quality of life examining body abnormality appearance

HRQOL questionnaire:

It was held using the Organization's WHOQOL-BREF quality of life assessment [7]**,** An Arabic translation was used**.** The questionnaire consisted of 26 items but one item about appreciation of sexual life was discarded putting into consideration the young age of the studied group. The questionnaire was administered to both patients themselves, if they had enough reading ability. In younger patients, we interviewed them with the help of the available parent. The investigator himself will explain each question. The items assessing four main domains that cover the aspects proposed to judge QOL. The assessed domains included:

• ***Physical health:*** Feeling that physical pain prevents from doing what needed by the patient, the need for medical treatment to function in daily life, having enough energy for everyday life, being satisfied with sleep, ability to perform daily living activity and capacity for learning

• ***Psychological health:*** The patient's ability to accept his/her bodily appearance, how much the patient enjoys life, patient's ability to concentrate, patient's satisfaction with him/herself, feeling that life is meaningful, and how often the patient has negative feelings such as blue mood, despair, anxiety and depression.

• ***Social relationships:*** Satisfaction with personal relationships and satisfaction with support taken from patient's friends.

• ***Environmental domain:*** How safe the patient feels in his/her daily life including: satisfaction with physical environment of the patient, satisfaction with the conditions of patient's living place, satisfaction with transport, satisfaction with the access to health services, having the opportunity for leisure activities, the availability of the information that the patient needs in day-to-day life and how feeling safe in the daily life.

Scoring and Classification System:

- WHOQOL-BREFF

The four domain scores denote an individual's perception of QOL in each particular domain. Scores are scaled in a positive direction, with higher scores denoting higher QOL. Items were related on a 5-point Likert scale and the raw scores obtained were transformed twice. The first converts' raw scores to range between 4-20, and the second converts domain scores to a 0-100 scale for ease of interpretation and comparison with the WHOQOL-100 according to instructions given in the user's manual.

Scores were calculated according to the standard method as instructed in the WHOQOL Brief manual. The mean score of items within each domain was used to calculate the domain score. Instructions for checking data and computing domain scores were used. Higher score indicates better health.

Ethical considerations:

Official approval of relevant authorities was taken before the start of the study. The objective of the study was explained for the parents, and then verbal consent was obtained from each child. Approval to carry research was obtained from the Ethical Committee of Faculty of Medicine, Zagazig University. Participation in the study was voluntary. No incentives were provided. Confidentiality of data was insured. There was no conflict of interest.

Statical analysis

Data were coded and entered using the statistical package SPSS version 23. Data were summarized using mean, standard deviation, median, minimum and maximum for quantitative variables and frequencies (number of cases) and relative frequencies (percentages) for categorical variables. Comparisons between groups were done using unpaired t test when comparing 2 groups, analysis of variance (ANOVA) with multiple comparisons and post hoc test when comparing more than 2 groups. For comparing categorical data, Chi square (χ^2) test was performed. Exact test was used instead when the expected frequency is less than 5. Correlations between quantitative variables were done using Pearson correlation coefficient. P-values $\leq$ 0.05 were considered statistically significant.

RESULTS

Table (1) illustrated socio-demographic characteristics of the studied group. The study included 392 patients with SS; 223 of them were females

(56.89%) and 169 of them were male (43.11 %) with age ranging between 12 to 18 years. The mean ± SD age of the patients was 15.77 ± 1.41 years. Number of children in urban was 191(48.72 %) and in rural was 201 (51.28%). in preparatory schools were 199 (50.77%) and in secondary schools were 193 (49.23%). Child order ranged from 1-5 with a mean of 2.41 ± 1.01. Number of children in the family ranged from 1-6 with a mean of 3.87 ± 1.19.

Table (2) showed that mean of height of patients was 143.28 ± 4.90 cm, mean of their weight was 44.41 ± 5.18 kg and mean of body mass index was 23.20 ± 3.82 kg/m^2.

Table (3) showed that concerning family history, more than 2/3 of the children with SS had negative consanguinity. 1.5% was with positive family history of a similar conditions and 15 % had positive family history of chronic disease e.g. HTN & DM.

The mean value of physical domain was 67.40 ± 18.10. The mean value of psychological domain was 56.17 ± 17.64. The mean value of social domain was 76.89 ± 12.91 (Table 4).

The data that are presented in table (5) described a comparison of sex groups (males and females) in relation to different domains among cases but it did not reach statistically significant difference**.**

The data that are presented in table (6) described a comparison of age groups (preparatory and secondary) in relation to different domains among cases but it did not reach statistically significant difference**.**

Table (1): Socio-demographic characteristics of the studied group

		N	%
Sex	**Female**	223	56.89
	Male	169	43.11
Residence	**Urban**	191	48.72
	Rural	201	51.28
Age (years)	**Preparatory**	199	50.77
	Secondary	193	49.23
Age (years)	**Mean ± SD**	15.77 ± 1.41	
Number of children in the family	**Mean ± SD**	3.87 ± 1.19	
Child order	**Mean ± SD**	2.41 ± 1.01	

SD: standard deviation

Table (2): Characteristics of children with SS according to the anthropometric measures

	Mean	±	SD
Height (cm)	143.28	±	4.90
Weight (kg)	44.41	±	5.18
BMI (kg/m^2)	23.20	±	3.82

Table (3): Family history parameters that affect QOL among children with SS (n 392)

		N	%
Consanguinity	**Positive**	91	23.21
	Negative	301	76.79
Family history of same SS case	**Positive**	6	1.53
	Negative	386	98.47
Family history of chronic disease	**Positive**	60	15.31
	Negative	332	84.69

Table (4): WHOQOL-BREF quality of life assessment of the patients

Domain	Mean	±	SD
Physical domain	67.40	±	18.10
Psychological domain	56.17	±	17.64
Social domain	76.89	±	12.91
Environmental domain	61.30	±	18.94

Table (5): Sex distribution of cases of SS in relation to different WHO QOL domains

Domain	Sex		P value
	Female	Male	
Physical	66.12 ± 14.31	67.30 ± 16.22	0.446
Psychological	54.11 ± 17.28	56.61 ± 16.67	0.151
Social	73.55 ± 16.47	76.35 ± 14.69	0.082
Environmental	58.19 ± 15.44	60.19 ± 16.54	0.219

QOL: quality of life; **SD:** standard deviation

Table (6): Age distribution at children with SS in relation to different WHO QOL domains

Domain	Age		P value
	Preparatory	Secondary	
Physical	65.89 ± 13.88	64.11 ± 14.90	0.222
Psychological	57.66 ± 14.12	55.78 ± 17.98	0.250
Social	78.71 ± 14.15	79.20 ± 13.69	0.728
Environmental	60.77 ± 15.80	62.97 ± 9.78	0.099

DISCUSSION

regarding socio-demographic characteristics of the studied children, our study included 392 patients with SS; 223 of them were females (56.89%) and 169 of them were males (43.11 %) with age ranging between 12 to 18 years. The mean age of the patients was 15.77 ± 1.41 years. Number of children in urban was 191 (48.72 %) and in rural was 201 (51.28%), in preparatory schools was 199 (50.77%) and in secondary school was 193 (49.23%). Child order ranged from 1-5 with mean of 2.41 ± 1.01. Number of children in the family ranged from 1-6 with mean of 3.87 ± 1.19.

Garganta and Bremer [8] showed that a comprehensive history starting in the prenatal and perinatal periods should be obtained. Emphases of the history include maternal health and habits during pregnancy, the duration of gestation, birth weight and length and growth pattern. It is generally recognized that babies of low birth weight with persistent postnatal SS do not have a favorable stature outcome**.**

Our study showed that regarding family history, more than 2/3 of the children with SS had negative consanguinity. While, 1.5% had positive family history of a similar condition and 15 % had positive family history of chronic disease e.g. HTN & DM. **Rogol and Hayden** [9] showed that familial or genetic SS is most often a normal variant, termed familial or genetic SS. These individuals usually have low-normal growth velocity throughout life. The otherwise normal growth velocity generally distinguishes these children from those with pathologic causes of SS**.** A family history of consanguinity might suggest a possible autosomal recessive condition. The presence of medical problems in the family would call for collection of detailed family history information, such as celiac disease and other gastrointestinal problems, kidney disease, and endocrinal disease such as growth hormone deficiency or hypothyroidism [10]**.**

Variants in genes that code for RNA-independent pseudo uridine synthases have been shown to result in a monogenic disorder. Recessively inherited PUS1 (MIM: 608109) pathogenic variants cause defective oxidative phosphorylation resulting in progressive mitochondrial myopathy and sideroblastic anemia (MLASA syndrome). In addition, growth delay, secondary microcephaly, and intellectual disability have been reported in multiple individuals [11]**.**

Family history is a significant resource for clues pertaining to a possible diagnosis of the cause of SS. As previously discussed, the father's and mother's heights are essential in defining the expected height of the child. The ages of puberty in the father and menarche in the mother are important when evaluating an adolescent for constitutional growth delay. In a 3-generation family history, the heights of siblings, grandparents, uncles and aunts, and 1st-degree cousins are all important in understanding familial growth patterns. The family's ethnicity may suggest familial SS [10]**.**

Regarding children with SS according to the anthropometric measures in our study, the mean value of height of patients was 143.28 ± 4.90 cm, mean value of their weight was 44.41 ± 5.18 kg and mean value of body mass index was 23.20 ± 3.82 kg/m^2.

Endocrine causes are classically associated with being overweight for height. In appropriately treated children with growth hormone deficiency or congenital hypothyroidism, puberty and final adult height are within the normal range among treated cases [9]**.**

In addition to increasing linear growth, improvement in health-related quality of life (HRQOL) is an important end point in the treatment of short statured youth. Hence, condition-specific psychometric valid instruments that adequately assess HRQOL are needed. We aimed to confirmatory examine the psychometric performance of the Quality of Life in Short Stature Youth (QoLISSY). Questionnaire was used in a previously reported prospective randomized open-label trial [12].

Voss stated that most reports on short children's school performance have also been based on clinic-referred samples. These studies commonly report academic underachievement in spite of average intelligence, but are likely to reflect specific neurocognitive deficits associated with specific syndromes, rather than the psychosocial consequences of SS. Importantly, it has been shown that within clinic-referred populations the problems of academic achievement are not related to height, nor are they remedied by GH therapy [13].

Wheeler *et al.* [14] found that children with SS have mean test scores within the range of normal for intelligence, academic achievement, and behavior (ie, within 1 SD of the mean). However, among the studies that directly compared short children with average-height controls who were otherwise similar to the short children most found that short children had significantly lower academic achievement test scores or a greater likelihood of low scores than controls. Similar results were found in a number of studies that evaluated intelligence**. Stratford *et al.*** [15] studied the relationship between SS and school performance in Netherland. It was examined by comparing an unselected cohort of 140 short children (below 3rd centile) aged between 7 and 9 years with 140 control children of normal height (10th-90th centiles). The short children had unimpaired self-esteem and normal patterns of behavior, but a tendency towards hyperactivity and poor concentration. Their IQ scores were normal, but attainment, especially in reading, was low. The underachievement observed among short children was largely attributed to the low socio-economic status of this group.

Differences according to socio-demographic characteristics were inspected for information about

the potential effects of age and gender on scale scores to be taken into consideration regarding scoring and clinical interpretation in future studies. Differences in mean scale scores between age groups (8–12 and 13–18 years) were only present in the Physical scale of the child self-report (t (47) =−2.55, p = 0.014, α = 0.05). Younger children (M = 74.49 ± 17.84) reported more limitations in their perceived physical QoL than adolescents (M = 85.58 ± 15.57) [16]

Regarding differences between gender, our results showed higher scores for emotional aspects of QoL for boys (M = 85.75 ± 15.80) than for girls (M = 72.56 ± 18.85; t (47) = −2.66, p = 0.11). In the parent report, significant differences between boys and girls were present in the three QoL subscales as well as in the total QoL score (t (54) = −2.23, p = 0.030). Parents of boys (M = 79.58 ± 14.84) reported their children to have a significantly better QoL than parents from girls (M = 70.07 ± 17.06) [16]

Our results showed that regarding WHOQOL-BREF quality of life assessment of the patients, the mean of physical domain was 67.40 ± 18.10. The mean of psychological domain was 56.17 ± 17.64. The mean of social domain was 76.89 ± 12.91. When comparing age and sex groups (males and females) in relation to different domains among cases, it did not reach statistically significant difference.

Silva *et al.* [17] suggested that children who were treated and who achieved normal height reported better QoL compared to those untreated and with current short stature. Parents of children with idiopathic short stature and current short stature presented greater caregiving stress than parents of children with growth hormone deficiency and achieved normal height. Children's better psychosocial functioning was indirectly associated with parents' better QoL, via less caregiving stress, and these links were invariant across diagnoses, treatment status, and current height deviation**.** These results suggest that, along with growth hormone treatments, multidisciplinary interventions in pediatric endocrinology should be family-centered, by targeting both the children's psychosocial functioning and the parents' stress, in order to improve individual and family adaptation [17].

On contrary to our results, **Bullinger *et al.*** [18] found a significant differences between the groups based on height were found in the following scales: Physical (p = 0.043) Social (p = 0.009) and Emotional (p = 0.044), confirming that taller children have better quality of life, as would be expected. The total score provided similar evidence of discriminated validity (p = 0.035). The parent-report version analysis yielded comparable results in that group differences based on height. Significant differences were found for the Physical (p = 0.001), Social (p = 0.001), the QoL and Total Score (p = 0.003), but failed to reach significance in the Emotional scale. The different results may be due to using a different questionnaire.

This was also supported in a previous study that showed a significant impact of current height deviation on coping behaviors and HRQOL of children/adolescents with SS, suggesting that effects of height deviation on psychological problems could be indirect, through lower HRQOL scores [19]**.**

CONCLUSION

Pediatric patients with SS have lower HRQOL. Social domain is the most affected among SS children.

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