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Health related quality of life is associated with gastroesophageal reflux symptoms in overweight children

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Abstract

Objectives: The association between obesity and gastroesophageal reflux disease (GERD) is well-established in adults; however, data in pediatric population is scarce. Our study aimed to assess the association between GERD and health-related quality of life (HRQoL) in overweight children.

Methods: From April to August of 2020, we included children aged 7–18 years who attended the Endocrinological Outpatient Clinic at the Paediatric Institute, University of Debrecen, Hungary. The participants completed two questionnaires: the Pediatric Gastroesophageal Reflux Disease Symptom Questionnaire (PGSQ) and the HRQoL questionnaire (PedsQL). Based on the criteria of the World Health Organization (WHO), the patients were categorized into two groups: an overweight or obese group and a group with normal weight.

Results: A total of 107 children (51 % female, mean age 13.2 years, 46 % overweight or obese) completed the questionnaires. The median PGSQ score was similar in both groups (4.0 (IQR: 1.0–7.8) vs. 3.0 (IQR: 1.0–7.0), $p=0.6$). However, the total PedsQL score was significantly lower in the children with overweight or obesity compared to those with normal weight (80.1 (71.1–91.0) vs. 88.0 (76.1–94.6), $p=0.031$). The PedsQL score was lower among overweight patients with GERD symptoms than that of normal-weight patients without GERD symptoms.

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Conclusions: Our findings highlight the importance of raising awareness about GERD to enhance the HRQoL and prevent long-term complications in obese children.

Keywords: obesity; gastroesophageal reflux disease; quality of life; children

Introduction

The relationship of gastroesophageal reflux disease (GERD) and obesity has been accepted and established in adults [1–3]. However, much less data is available in childhood, though the increasing prevalence of pediatric obesity may also contribute to the prevalence of GERD and the rise of long-term complications of GERD.

In adults, one of the most important risk factors for GERD is obesity, and the first line therapy includes lifestyle change and weight loss according to the current guidelines [4]. Obesity is associated with higher intraabdominal pressure and increased transient lower esophageal sphincter relaxation that are the major triggers of GERD [5]. In addition, it has been shown that obesity is associated with GERD related complications, as esophageal adenocarcinoma, and Barrett's esophagus [1, 5, 6].

In children, lifestyle changes and weight loss are also among the first line therapy in GERD, though the evidence is low [7]. The data on the prevalence of GERD and obesity in children are sparse and inconclusive due to heterogenous methodology. Some studies did not find significant difference in the frequency of GERD between children with overweight and with normal weight [8, 9]. Meanwhile, Stordal et al. reported an association between BMI and GERD symptoms [10]. Furthermore, Quitadamo et al. assessed the prevalence of GERD in children with obesity and normal weight via questionnaire and reported obesity as a risk factor for GERD symptoms [11].

Obesity is not only linked to metabolic syndrome and serious morbidities, but it also affects mental health and quality of life in children. Several studies demonstrated lower health related quality of life (HRQoL) in children with obesity and overweight [12–17], especially scores of social and physical dimensions were reduced. However, data on

HRQoL in obese children with GERD symptoms are lacking, only one study reported that obese children with GERD have lower HRQoL than obese children without GERD symptoms [18].

In order to fulfil the knowledge gap in the field of relationship of GERD and obesity in children our primary aim was to compare GERD symptoms in obese and non-obese children. The secondary aim was to evaluate the HRQoL of obese children with or without GERD.

Materials and methods

For this descriptive, single-center cohort study, we consecutively enrolled children under 18 years who agreed to participate and signed informed consent in our study at Pediatric Endocrinological Outpatient Clinic, University of Debrecen, Hungary. Children were recruited from April 2020 to August 2020. We excluded children younger than seven years and children with BMI under $-2SD$.

Questionnaires

All children and their parents were requested to complete two questionnaires to assess the presence and severity of GERD symptoms, as well as the impact on their quality of life. The Hungarian adaptation of the Pediatric Gastroesophageal Reflux Disease Symptom and Quality of Life Questionnaire (PGSQ-SYM) [19] was employed for evaluating GERD symptoms. This questionnaire consists of 15 items, which are rated based on the frequency of occurrence over the past week using a 5-point scale: none (0 days), one or 2 days, three or 4 days, five or six days, and every day (seven days). A cut-off score of greater than seven on the PGSQ is used to define GERD [20]. In addition, the Pediatric Quality of Life Inventory (PedsQL) was utilized to assess the HRQoL [21]. The PedsQL generic core scale comprises four domains, with a total of 23 items: physical functioning (eight items), emotional functioning (five items), social functioning (five items), and school functioning (five items). Scores on the PedsQL are transformed to a scale ranging from 0 to 100, with higher scores indicating better quality of life.

Data collection

Demographic data including age, sex, body height and weight, as well as any concomitant disease were collected for all participants from the medical records. BMI was calculated as weight (kilograms) divided by the square of the height (meters). The BMI-for-age standard deviation was calculated using the sex-specific BMI-for-age growth charts developed by the Hungarian Longitudinal Growth study [22]. Overweight and obesity were defined based on the criteria established by the World Health Organization (WHO) [23]. Children were categorized as normal weight (BMI-for-age -1.9 – 0.9 standard deviation), overweight (BMI-for-age greater than $+1.0$ standard deviation), and obese (BMI-for-age greater than $+2.0$ standard deviations).

Statistical analysis

The comparison of median scores for HRQoL and PGSQ between two groups, namely children with normal BMI (normal-weight group) and children with obesity or overweight (overweight group), was conducted. Additionally, a subgroup analysis was performed to compare GERD symptoms and HRQoL specifically in children with obesity or overweight and normal weight.

Continuous variables with normal distribution were expressed as means and standard deviations, while non-normal continuous variables were presented as medians and interquartile ranges. The normality of the data was assessed using the Kolmogorov–Smirnov test. Statistical analyses were performed using appropriate tests depending on the distribution of the variables. The Mann–Whitney U-test was utilized for non-normally distributed and independent t-test was applied for normally distributed variables, respectively. Categorical variables between normal weight and overweight or obese patients with endocrine diseases were assessed by chi-square test. Statistical significance was defined as $p < 0.05$.

The statistical analyses were conducted using the IBM SPSS statistical package version 25 and GraphPad Prism version 8.

Ethical considerations

This study was approved by the Regional and Institutional Research Ethics Committee of University of Debrecen. Informed consent was obtained from all participants.

Results

Patients

Altogether 107 children returned PGSQ-SYM questionnaire and PedsQL survey (female: 55 (51 %), mean age: 13.2 ± 3.04 years; normal weight: 59 (55 %), overweight or obese: 48 (45 %)). All questionnaires were filled out correctly; there were no missing or doubtful reply. In children with obesity or overweight, the mean BMI was 29.1 kg/m^2 (± 5.5), while children with normal weight the mean BMI was 18.9 kg/m^2 (± 2.8). Most patients (86/107, 80 %) had known underlying endocrine disease at enrolment (Table 1).

GERD symptoms and PedsQL in children with obesity or overweight and with normal weight

We compared the median scores of the PedsQL and PGSQ-SYM questionnaires between the two groups. The median score of PGSQ-SYM questionnaire did not differ between children with obesity or overweight and with

Table 1: Demographics and baseline characteristics of included patients.

	Children with normal weight (n=59)	Children with overweight or obesity (n=48)	p-Value
Female (n, %)	27 (46 %)	28 (58 %)	–
Age (years, mean±SD)	13.1±3.0	13.3 ±3.1	0.74
BMI z score (mean±SD)	−0–16±0.6	3.1±1.6	<0.0001
Concomitant disease (n, %)	49 (83 %)	37 (77 %)	0.44
Autoimmune thyroiditis (n, %)	10 (17 %)	14 (29 %)	0.13
Hypothyroidism (n, %)	5 (9 %)	8 (17 %)	0.19
Type 1 diabetes mellitus (n, %)	18 (31 %)	10 (21 %)	0.26
Hypopituitarism	4 (7 %)	2 (4 %)	0.8
Short stature	10 (17 %)	2 (4 %)	0.07
Late onset congenital adrenal hyperplasia	1 (1.7 %)	0	0.8
Diabetes insipidus	1 (1.7 %)	0	0.8

Most patients (80 %) had known underlying endocrine disease at enrolment: autoimmune thyroiditis, hypothyroidism, type 1 diabetes mellitus.

normal weight (4.0 (IQR: 1.0–7.8) vs. 3.0, (IQR: 1.0–7.0), $p=0.6$). The rate of GERD was not different in the two groups (14/48 vs. 16/58, $p=0.65$). It is of note, that parents were also asked to complete PGSQ-SYM, and the median of the parental questionnaire was significantly lower than the median of the questionnaire score filled out by children (1.0 (IQR: 0.0–5.0) vs. 3.0 (IQR: 1.0–7.0), $p=0.026$) (Figure 1).

However, the median of the PedsQL total score was significantly lower in children with obesity or overweight than in the group with normal weight (80.1 (71.1–91.0) vs. 88.0 (76.1–94.6), $p=0.031$), in addition, social and physical function domains were also significantly lower (Table 2).

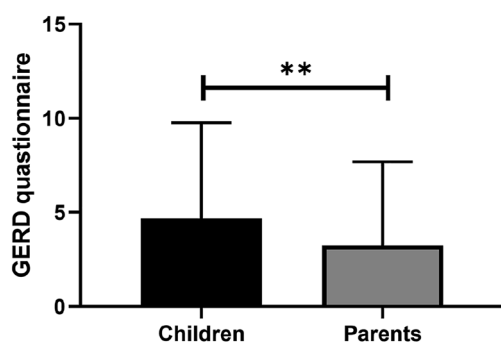


Figure 1: PGSQ score in questionnaire completed by children and parents. The median score of the parental questionnaire was significantly lower than the median score of the questionnaire score filled out by children.

Table 2: Comparison of PedsQL scores in children with overweight or obesity and normal weight.

	Children with overweight or obesity (n=48)	Children with normal weight (n=59)	p-Value
PedsQoL – total (median, IQR)	80.1 (71.1–91.0)	88.0 (76.1–94.6)	0.031*
PedsQoL – physical function (median, IQR)	87.5 (78.1–96.1)	93.8 (84.4–100.0)	0.037*
PedsQoL – emotional function (median, IQR)	80.0 (60.0–88.8)	80 (65.0–95.0)	0.233
PedsQoL – social function (median, IQR)	92.5 (75.0–100.0)	100.0 (90.0–100.0)	0.010*
PedsQoL – school function (median, IQR)	80.0 (60.0–90.0)	80.0 (70.0–95.0)	0.167

The median of the PedsQL total score, social and physical function domains was significantly lower in children with overweight or obesity than in children with normal weight.

Relationship between quality of life, obesity and GERD in children

The median PedsQL score was compared in four groups: (1) overweight or obese children with GERD symptoms; (2) overweight or obese children without GERD symptoms; (3) normal-weight children with GERD symptoms and (4) normal-weight children without GERD symptoms. Overweight or obese children with GERD symptoms had significantly lower total PedsQL score compared to the other three groups (69.0 (IQR: 63.0–80.4) vs. 85.3 (IQR: 75.3–94.4) vs. 85.3 (IQR: 74.5–92.4) vs. 89.1 (IQR: 81.5–94.6)) (Supplementary Table 1 and Figure 2). Children with GERD symptoms exhibited significantly lower PedsQL score compared to children without GERD symptoms, regardless their BMI. Furthermore, children with overweight or obesity had lower PedsQL score than children with normal weight independently from their GERD symptoms.

Discussion

Hereby, we presented GERD symptoms and HRQoL in children with overweight and obesity. We showed that the HRQoL is lower in children with overweight or obesity and GERD can contribute to the lower HRQoL. It is of note that parents reported less frequently GERD symptoms than children.

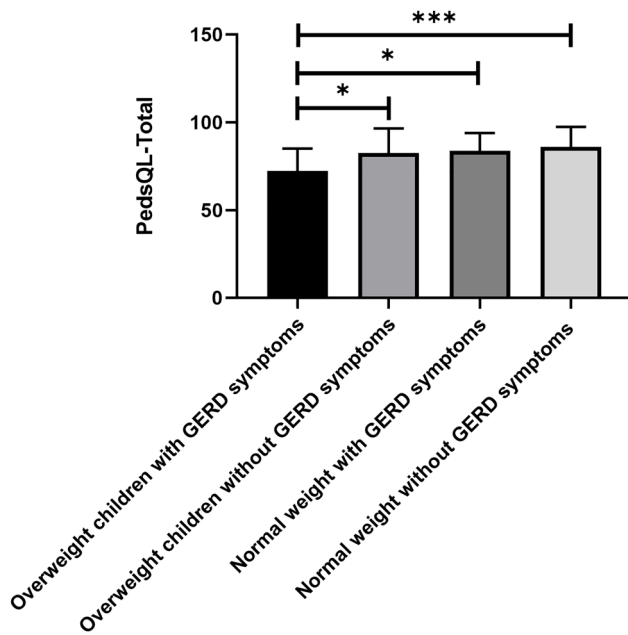


Figure 2: Health related quality of life in normal-weight and overweight or obese children with or without GERD symptoms. The median PedsQL score was compared in four groups: (1) overweight or obese children with GERD symptoms; (2) overweight or obese children without GERD symptoms; (3) normal-weight children with GERD symptoms and (4) normal-weight children without GERD symptoms. Overweight or obese children with GERD symptoms had significantly lower total PedsQL score compared to the other three groups. Children with GERD symptoms exhibited significantly lower PedsQL score compared to children without GERD symptoms, regardless their BMI. Furthermore, overweight or obese children had lower PedsQL score than normal-weight children independently from their GERD symptoms.

Previous studies reported frequency of GERD in children with overweight or obesity between 13 and 38 % [8, 10, 18, 24, 25]. In a recent study, Al-Agha et al. demonstrated the frequency of GERD diagnosed via pH-metry was 22 %, similar to previous studies with different methodology [26]. The association between GERD and obesity has been established in adults; however, in children the data are controversial. Some studies based on the results of retrospective analysis of endoscopy and biopsy did not find association between overweight and GERD symptoms in pediatric populations [8, 9]. Meanwhile, studies mostly based on questionnaires showed a relationship between overweight and GERD in children [10, 11, 24, 25, 27]. In our study, the frequency of GERD in children with overweight and obesity was quite low (16 %) and did not exceed the frequency in children with normal weight. Though, the mean PGSQ score was non-significantly higher in children with overweight and obesity than in children with normal weight suggesting that children with overweight and obesity may have more severe GERD symptoms. The lack of difference can be explained by the relatively

low number of cases in our cohort and the lack of objective diagnostic approach of GERD.

Additionally, it has to be highlighted that parents reported less GERD symptoms compared to children. This observation suggests that children may have difficulty expressing their complaints or that these symptoms are underestimated by their environment. Given the potential complications associated with long-term, unmanaged GERD, this finding underscores the importance of raising awareness about GERD in children with overweight and obesity.

The HRQoL of children with overweight and obesity is known to be affected compared to children with normal weight. However, HRQoL in overweight or obese children with GERD symptoms was evaluated in only one study previously. Quitadamo et al. reported that the HRQoL (PedsQL) mean score was significantly lower among obese patients with GERD symptoms than obese patients without GERD, and healthy non-obese children [18]. A similar tendency was apparent in our cohort; however, the difference was not significant between overweight and obese children with or without GERD symptoms. However, the HRQoL was significantly better in children with normal weight without GERD symptoms.

Obesity can trigger GERD via different mechanisms, such as mechanical and humoral factors. The excessive abdominal fat contributes to increased intra-abdominal pressure, and to the risk of hiatal hernia resulting in disrupted antireflux mechanism. Additionally, the visceral adipose tissue produces several cytokines that can mediate esophageal inflammation and promote the impairment of esophageal mucosal barrier [28]. Wu et al. described a correlation between higher BMI and waist circumference and increased transient relaxations of the lower esophageal sphincter [29]. Quitadamo et al. has investigated the mechanism of GERD in obese children [18]. They found that gastric emptying time was significantly delayed in obese children with increased reflux events. Furthermore, both symptomatic and asymptomatic obese children had a worse HRQoL compared with healthy patients, highlighting that asymptomatic GERD can occur even in childhood, not only in adults [30, 31].

Our study has certain limitations related to its study design, including being a single-center, cross-sectional study. Additionally, the relatively small number of our cohort may introduce some uncertainty in our findings. Though PGSQ has been applied in several studies, questionnaires are not recommended to assess GERD in everyday practice [7]. Furthermore, waist circumference that is considered as a marker of visceral adiposity may have been beneficial to record and analyze the relationship between GERD and overweight.

There is a lack of robust data on the prevalence of GERD in children with overweight and long-term consequences of

pediatric GERD are missing. This highlights the need for high-quality prospective studies that can explore the relationship between GERD and obesity in childhood, as well as investigate the long-term outcomes associated with this condition. It is essential to address these limitations and conduct further research to improve our understanding of GERD in children with obesity and its potential long-term effects.

In conclusion, our study showed that parents may underestimate symptoms of GERD in children. The HRQoL of overweight or obese children with GERD is lower than children with normal weight without GERD symptoms. This study emphasizes the importance of awareness of GERD symptoms in children with overweight or obesity to improve HRQoL and to prevent long-term complications of uncontrolled GERD, such as Barrett's esophagus and esophageal adenocarcinoma.

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Research ethics: The local Institutional Review Board deemed the study exempt from review.

Informed consent: Informed consent was obtained from all individuals included in this study, or their legal guardians or wards.

Author contributions: The author(s) have (has) accepted responsibility for the entire content of this manuscript and approved its submission.

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Data availability: The raw data can be obtained on request from the corresponding author.

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