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REGULAR ARTICLE

Parentally reported early childhood upper gastrointestinal symptoms alleviate at school age

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Abstract

Aim: This study estimated follow-up outcomes for children presenting with troublesome upper gastrointestinal (GI) symptoms in early childhood.

Methods: We identified from our upper endoscopy registry children with undefined GI symptoms having undergone an oesophagogastroduodenoscopy to rule out oesophagitis at a median age of 2.6 years in 2006–2016. We included only those with normal findings. In early 2020, we performed a National Patient Data Repository and Prescription Service review to note patients' current GI symptoms, medications and medical consultations. We also employed a study-specific questionnaire with a validated quality-of-life measure (the PedsQL).

Results: After a median of 7.9 years of follow-up, the children ($n = 199$) had a median age of 10.6 years. Medical consultations related to upper GI symptoms were rare. However, parents reported recurrent GI symptoms in 24% of the children, and 41% followed a specific diet. Regular anti-acid medication was in use in 3.5% of the cohort, more often when with a predisposing condition for reflux disease. The current quality of life was good.

Conclusion: Although some upper GI symptoms may persist after early childhood, patients without diseases predisposing to reflux disease have a good quality of life without GI-related morbidity in school age.

KEYWORDS

endoscopy, gastrointestinal symptoms, gastro-oesophageal reflux, health-related quality of life, long-term outcome

1 | INTRODUCTION

Recurrent upper gastrointestinal (GI) symptoms, such as abdominal pain, gastro-oesophageal reflux (GOR) and vomiting, are common in the paediatric age group and often cause parents of young children to seek medical advice.¹ Such children may be at risk of being

exposed to unnecessary and inexpedient medical procedures² as clinicians' knowledge of, and adherence to, published guidelines governing diagnosis of functional GI symptoms is patchy.³ Although otherwise healthy children seem less at risk of organic disease, clinicians prescribe anti-acid medications widely to treat symptoms attributed to troublesome upper GI symptoms across all paediatric age

Abbreviations: GI, gastrointestinal; GOR, gastro-oesophageal reflux; GORD, gastro-oesophageal reflux disease; IQR, interquartile range; OGD, oesophagogastroduodenoscopy; QoL, quality of life.

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groups.^{4–6} However, the benefits of such medications are inconclusive, particularly in infants,^{7,8} and various long-term harms related to prolonged proton pump inhibitor (PPI) medication have been reported.^{9,10} Moreover, in our previous study, we found that in young children with non-specific symptoms, oesophagogastroduodenoscopy (OGD) findings were scarce.¹¹

Apart from physical symptoms, psychological factors such as heightened symptom expectations, anxiety or depression, or beliefs relating to exposures that might trigger symptoms have been associated with subjective symptom perception¹² and may affect parents' perception of their child's symptoms.¹³ This poses a challenge to clinicians, as also prognostic factors related to common early childhood non-specific upper GI symptoms are unclear.¹⁴ Also, there is a lack of instruments for assessing, for example, pain in young children.¹⁵

To fill in gaps in current knowledge, we evaluated school-age outcomes of children who had presented with early childhood troublesome upper GI symptoms without defined aetiology.

2 | METHODS

For this follow-up study, we included children who had undergone a primary OGD to rule out oesophagitis at a median age of 2.6 years and who had been identified in our previous study ($n = 268$).¹¹ The primary OGDs had been performed in 2006–2016 in Children's Hospital, University of Helsinki, the major tertiary care hospital in Finland. In early 2020, we had access to files of 254/268 children. Of these, we excluded patients with positive findings in primary OGD ($n = 55$). Thus, the total number of included children was 199 (all with normal findings), including 176 patients with GI symptoms and 23 patients who had undergone OGD due to non-specific respiratory symptoms (Figure 1). We further divided the 176 GI patients into two groups: children without known GOR-promoting conditions ($n = 135$) and children with known GOR-promoting conditions (non-GI) such as neurological disability ($n = 41$).¹⁶ Patients with earlier respiratory symptoms are reported as a separate group.

2.1 | Registry-based data

We reviewed data from our hospital patient charts for the whole follow-up period. In addition, using the electronic National Patient Data Repository, we noted the number of contacts with the healthcare system addressing current upper GI complaints within the last 2 years. The Repository is accessible to both patients and healthcare professionals, and professional usage is allowed with patient's/guardian's permission. Permission is routinely asked when the patient signs in for the first healthcare contact, and patients/guardians seldom deny it. In addition, we reviewed all anti-acid medication prescriptions written over the previous 2 years using the National Prescription Service. This database is accessible to all licensed physicians.

Key Notes

- We estimated the follow-up outcomes of children in whom parental reports of severe upper GI symptoms had led to oesophagogastroduodenoscopy at a median age of 2.6 years resulting in normal findings.
- After a median of 8 years, parents reported GI symptoms in 24% of their currently school-age children.
- In only few of these children, such symptoms had necessitated medical consultations or anti-acid medications during the last 2 years.

2.2 | Follow-up survey

We identified families who had noted Finnish as their native language and sent them three rounds of invitation letters to participate in an electronic follow-up survey on child's current well-being and GI-related quality of life (QoL). We asked the parents to contact the author (N.H.) via e-mail if they wished to participate in the study. The Internet-based study questionnaire addressed to parents included 44 items on patient demographics, the child's current upper GI symptoms and diet. Also, we ascertained the parent's perception of the child's current QoL by using the PedsQL GI Symptoms Scales and invited also children aged 8–17 years to fill in a child/teenager self-report (Figure 1). The PedsQL GI Symptoms Scales is a validated questionnaire with 74 items and includes GI symptoms and worry about symptoms domains.¹⁷ It uses a five-point Likert scale from 0 (never) to 4 (almost always), and scores are transformed on a scale from 0 to 100. Higher scores indicate better QoL. The questionnaire was professionally translated to and validated in Finnish for this study.

Written informed consent was obtained from all parents and children older than 8 years who responded to the follow-up survey. According to Finnish legislation, informed consent is not required for register-based studies. The study was approved by the Helsinki University Hospital's Ethics Committee (HUS/1743/2019).

2.3 | Statistical analyses

Data are presented as the median and interquartile range (IQR) or mean and range, if appropriate. We compared categorical data using the Mann-Whitney test or Fisher exact test and performed statistical analysis using GraphPad Prism version 9.0 for Windows (GraphPad Software, San Diego, CA, USA). The level of statistical significance was set at 0.05.

3 | RESULTS

Our follow-up study included 199 children, who all had undergone a primary OGD with normal findings at a median age of 2.6 years.

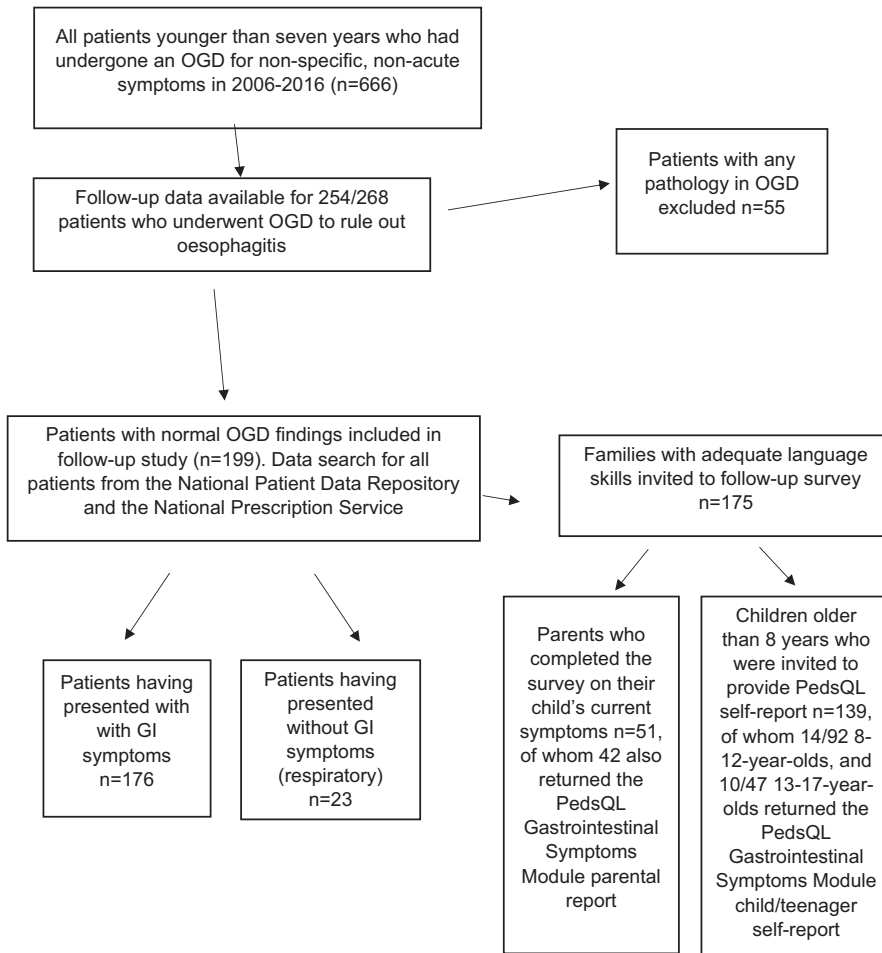


FIGURE 1 Flow chart on patient selection for the follow-up study on 199 children presenting with troublesome upper gastrointestinal (GI) or respiratory symptoms in early childhood. All had undergone a primary oesophagogastroduodenoscopy (OGD) at a median age of 2.6 years in a tertiary level Children's Hospital between 2006 and 2016

After a median follow-up time of 7.9 years, the children had a median age of 10.6 years. Patient characteristics are shown in Table 1.

median age of 10.4 years (IQR 8.4–13.5), comparable to the entire study cohort ($n = 199$).

3.1 | Follow-up data from the hospital patient charts, the national patient data repository and the prescription service

After the primary OGD, there were only a few visits to the healthcare system in most children, and upper GI complaints were seldom mentioned in patient charts. Also, based on the data from the National Prescription Service, anti-acid medications were seldom prescribed. However, 3.5% of the children had been prescribed long-term anti-acid medication. Current anti-acid medication use was significantly more common among children with predisposing conditions to GOR ($p = 0.005$, Table 2a).

3.2 | Follow-up questionnaire survey

We were able to reach 57/175 Finnish-speaking families (32.6%), and 51/175 parents (29.1%) returned the questionnaires regarding their child's current upper GI symptoms. The median follow-up time for survey participants was 7.9 years (IQR 5.1–10.2) after the primary OGD. The children were primarily male (58.8%) and had a current

3.2.1 | Current GI symptoms

Overall, parentally reported upper GI symptoms during the previous 3 months were common (24/51, 47.1%). Of these, 12/51 (23.5%) were reported to have symptoms weekly, and 2/51 (3.9%, both with predisposing condition to GOR) daily (Table 2b).

3.2.2 | Current diet

Several parents ($n = 27/51$, 52.9%) reported that dietary changes had helped with their child's upper GI symptoms, and 21/51 children (41.2%) were reported to have dietary restrictions, including milk- or gluten-free diets (Table 2b).

3.2.3 | Quality of life

A complete parental PedsQL GI Symptoms Scales report was available from 42/175 parents (24.0%). Child self-reports were available from 14/92 (15.2%) of the 8–12-year-olds and 10/47 (21.3%) of

TABLE 1 Background data on the study cohort

	All patients	Children with upper GI symptoms, no predisposing conditions for GOR	Children with upper GI symptoms and with a known predisposing condition for GOR	Children with respiratory symptoms attributed to GOR
No. of patients (%)	199 (100)	135 (67.8)	41 (20.6)	23 (11.6)
Male (%)	113 (56.8)	72 (53.3)	27 (65.9)	14 (60.9)
The leading symptom for OGD in early childhood (%)				
Vomiting or spitting up	116 (58.3)	88 (65.2)	28 (68.3)	0
Heartburn	26 (13.1)	21 (15.6)	5 (12.2)	0
Dysphagia or refusal to eat	14 (7.0)	12 (8.9)	2 (4.9)	0
Other (various non-specific symptoms)	43 (21.6)	14 (10.4)	6 (14.6)	23 (100)
Age at primary OGD, years, median (IQR)	2.6 (1.3–4.3)	2.5 (1.3–4.3)	2.7 (0.8–3.8)	3.0 (1.1–4.7)
No. of patients with anti-acid medication in use at some point before the primary OGD (%)	106 (53.3)	75 (55.6)	23 (56.1)	8 (34.8)
No. of patients using anti-acid medication continuously at the time of the primary OGD (%)	25 (12.6)	15 (11.1)	8 (19.5)	2 (8.7)

Note: The cohort of 199 children had undergone a primary oesophagogastrroduodenoscopy (OGD) for upper gastrointestinal (GI) or respiratory symptoms in 2006–2016, and all findings in OGD were normal.

Abbreviations: GOR, gastro-oesophageal reflux; IQR, interquartile range.

TABLE 2 A Registry data on current GI symptoms and anti-acid medication use

	All patients	Children with previous GI symptoms, no predisposing conditions for GOR	Children with previous GI symptoms and with a known predisposing condition for GOR	Children with previous respiratory symptoms who underwent OGD
No. of patients (%)	199 (100)	135 (67.8)	41 (20.6)	23 (11.6)
Age at follow-up, years, median (IQR)	10.6 (8.2–13.4)	10.6 (8.1–13.4)	10.4 (8.2–13.3)	10.7 (8.3–13.5)
Follow-up time years, median (IQR)	7.9 (5.3–10.1)	8.0 (5.3–10.0)	7.9 (5.4–11.1)	7.7 (5.2–10.9)
No. of children with upper GI symptom-related contacts in patient charts during the follow-up (%)	8 (4.0)	1 (2.6)	7 (17.1)	0
No. of patients treated in our hospital at the time of the follow-up (e.g. asthma, neurological conditions) (%)	73 (36.7)	36 (26.7)	27 (65.9)	10 (43.5)
No. of patients using anti-acid medication during the follow-up based on Prescription Service data (%)				
Continuous	7 (3.5)	2 (1.5) ^a	5 (12.2) ^a	0
Occasional	9 (4.5)	4 (3.0)	4 (9.8)	1 (4.3)

Note: Registry data on follow-up outcomes on 199 children who, in early childhood, had undergone a primary oesophagoduodenoscopy (OGD) for troublesome upper gastrointestinal (GI) or respiratory symptoms with normal findings. Patients are grouped according to leading symptoms at the time of the primary OGD and whether they had predisposing conditions for gastro-oesophageal reflux (GOR) or not.

Abbreviation: IQR, interquartile range.

^aSignificant difference when these two groups were compared ($p = 0.005$).

TABLE 2 B Background data of patients invited to a follow-up survey

	All patients	Children with previous GI symptoms, no predisposing conditions for GOR	Children with previous GI symptoms and with a known predisposing condition for GOR	Children with previous respiratory symptoms who underwent OGD
No. of parents with Finnish as their native language invited to follow-up survey on their child's current well-being (%)	175 (100)	119 (68.0)	36 (20.6)	20 (11.4)
No. of invited families who participated in the follow-up survey on current well-being (%)	51 (29.1)	38 (31.9)	7 (19.4)	6 (30.0)
No. of children with parentally reported upper GI symptoms at follow-up (%)	24 (47.1)	17 (44.7)	5 (71.4)	2 (33.3)
Daily symptoms	2 (3.9)	0	2	0
Weekly symptoms	10 (19.6)	10	0	0
No. of children with parentally reported food restriction (%)	21 (41.2)	14 (36.8)	5 (71.4)	2 (33.3)
Lactose-free	7 (13.7)	5	1	1
Milk-free	3 (5.9)	3	0	0
Gluten-free	6 (11.8)	4	1	1
Other	5 (9.8)	2	3	0
No. of subjects with Finnish as their native language invited to provide quality of life report (PedsQL GI Symptoms Scales) at follow-up (%)	175 (100)	119 (68.0)	36 (20.6)	20 (11.4)
Parents on their child	92 (100)	64 (69.6)	19 (20.7)	9 (9.8)
8-12-year-olds	47 (100)	32 (68.1)	8 (17.0)	7 (14.9)
No. of participants who returned the PedsQL GI Symptoms Scales questionnaire (%)	42 (24.0)	31 (26.1)	5 (13.9)	6 (30.0)
8-12-year-olds	14 (15.2)	11 (17.2)	2 (10.0)	1 (11.1)
13-17-year-olds	10 (21.3)	8 (25.0)	1 (12.5)	1 (14.3)

Note: Parents were asked to evaluate their child's current well-being and gastrointestinal (GI) symptoms and the quality of life related to them. In addition, children older than eight years were invited to self-report their current quality of life. We used the PedsQL GI Symptoms Scales for quality-of-life measurement. Patients are grouped according to leading symptoms and whether they had predisposing conditions for gastro-oesophageal reflux (GOR) or not at the time of primary oesophagostroduodenoscopy (OGD).
Abbreviation: PedsQL, pediatric quality-of-life inventory.

TABLE 3 Data on individual symptom module results of the PedsQL gastrointestinal symptoms scales quality-of-life (QoL) questionnaire

	Healthy children	Children 8-12-year-olds self-report	Teenagers 13-17-year-olds self-report	Parental reports for healthy children	Parental reports for 5-7-year-olds	Parental reports for 8-12-year-olds	Parental reports for 13-17-year-olds
No. of patients	14	10	10	7	24	11	11
Symptoms total score	88.6	89.5	89.2	90.0	79.4 ^{b,c}	87.9 ^b	89.6 ^c
Stomach pain and hurt	84.5	85.7	84.2	79.1	63.7	81.6	84.5
Stomach discomfort when eating	89.6	90.4	91.5	88.6	74.3	88.5	90.5
Food and drink limits	89.7	85.4	80.4	91.0	66.1	84.0	75.0
Trouble swallowing	95.6	91.7	92.5	96.5	95.2	92.7	92.4
Heartburn and reflux	90.6	86.2	88.2	93.3	72.9	83.6	88.7
Nausea and vomiting	91.6	96.9	93.1	92.1	84.8	94.4	94.6
Gas and bloating	83.3	79.8	77.5	86.9	71.0	79.0	82.5
Constipation	86.9	86.4	88.7	89.3	81.9	87.6	91.2
Blood in poop	96.3	99.1	98.8	96.3	96.4	97.9	98.9
Diarrhoea	94.3	93.4	96.8	94.8	87.8	91.4	97.7

Note: Data on the current quality of life. We invited a subgroup of 175 families with Finnish as their native language to take part in a follow-up survey. All children had undergone an oesophagogastroduodenoscopy for troublesome upper gastrointestinal or respiratory symptoms a median of 7.9 years ago. Data are shown as mean in each group and timeline asked in the previous month. The maximum score is 100, and higher scores indicate better health-related QoL and fewer symptoms. Values that are lower than the reported healthy children mean^a are shown in bolded font.

^aVarni JW, Bendo CB, Denham J, et al. PedsQL Gastrointestinal Symptoms Scales and Gastrointestinal Worry Scales in paediatric patients with functional and organic gastrointestinal diseases in comparison with healthy controls. *Qual Life Res.* 2015;24(2):363-378.

^bSignificant difference in parental reports of 5-7-year-olds and 8-12-year-olds ($p = 0.028$).

^cSignificant difference in parental reports of 5-7-year-olds and 13-17-year-olds ($p = 0.020$).

the 13–17-year-olds. Table 2b shows respondents according to the subgroups.

In general, GI-related QoL was good but slightly below the mean value reported for healthy children.¹⁸ The mean parent-reported PedsQL GI Symptoms total score was 86.9 (range 52.9–99.1). The results of individual symptom modules are shown in Table 3. Parents of 5–7-year-olds reported significantly lower scores than those reported by parents of 8–12-year-olds and 13–17-year-olds ($p = 0.028$ and $p = 0.020$, respectively). However, in the child–parent dyads, the results of parental and child/teenager self-report total scores and scores across individual modules were similar (data not shown).

4 | DISCUSSION

We conducted a follow-up study on children who had undergone a primary OGD because of troublesome upper GI (or respiratory) symptoms at a median age of 2.6 years but with normal findings. The upper GI symptoms without defined aetiology had a favourable outcome. After a median of 7.9 years of follow-up, at a median age of 10.6 years, the general outcome was good; although occasional upper GI symptoms were noted, long-term anti-acid medication was scarcely used, and GI-related QoL was generally reported as good. To date, data on the prognosis of early childhood non-specific upper GI symptoms are limited.^{14,19}

Based on the National Patient Data Repository data, among children without predisposing conditions to GOR, only a few had recent contacts with the healthcare providers because of upper GI complaints. However, among children with known predisposing conditions to GOR (primarily developmental problems or cerebral palsy-related neurological conditions), most (71%) were still reported to suffer from upper GI symptoms. The children who had been investigated for respiratory symptoms to help rule out oesophagitis had not developed upper GI symptoms during the follow-up and had very few health complaints in general. Our results are in line with previous research reporting that respiratory symptoms are not attributed to GOR.²⁰

Our cohort does not seem to overuse anti-acid medications, which shows good adherence to the international paediatric GORD guidelines.³ However, 3.5% of the children were currently using long-term PPI medication for symptoms attributed to GOR, while in 4.5%, anti-acid medication had been occasionally used within the last 2 years. Most of the children (56%) using PPI medication had a predisposing condition to GOR. We were unable to cover pharmaceuticals other than prescription medications, but in Finland, PPIs are not licensed for over-the-counter use in children. The increased use of PPI medication in children has raised concerns among paediatric gastroenterologists.¹⁰ Long-term PPI use has been associated with potentially harmful alteration of the gut microbiome,²¹ increased risk of inflammatory bowel disease²² and bacterial infections in the GI tract.⁵ Therefore, it is essential to restrain the medication for patients with objective proof of excessive acidic GOR.

In the subgroup participating in our follow-up questionnaire survey, the proportion of parentally reported current daily and weekly occurring upper GI symptoms was 24%. Perhaps, reflecting this also parentally reported food restrictions were common. In the general population, only 5–8% of children older than ten are reported to present with weekly GOR-related symptoms.²³ We were unable to specify the aetiology of the parent-reported symptoms, but multiple factors have been reported to influence parental perception of their child's symptoms.¹³ Symptom attributions are crucial in experiencing symptoms.¹² However, no studies have addressed parentally perceived upper GI symptoms in children, and in general, data on parental perception of their child's symptoms warrant further research.^{13,24} Also, here, a potential bias may exist because of the relatively low questionnaire return percentage (33%). The children who did not have current upper GI complaints may have felt the survey participation was not relevant.²⁵

The QoL measured here using the PedsQL GI Symptoms Scales was good. In most of the modules, as reported in Table 3, both the parent and child/teenager self-report scores were slightly lower than the previously reported healthy children's mean scores.¹⁸ Moreover, the younger the child was, the lower scores the parents reported. However, parentally reported PedsQL total scores in children diagnosed with GORD have been reported as 13% lower than in healthy controls.¹⁸

Our study's strengths include a large number of paediatric patients from a single tertiary level centre with few lost to follow-up. The choice of using the OGD registry to identify patients with upper GI symptoms was based on the severity of symptoms it entails. The National Patient Data Repository and the National Prescription Service data provided here are exceptional and conclusive. We had access to all public healthcare visits, including routine school nurse check-ups. As a limitation, the heterogeneity in patient chart documentation confers some ambiguity to our retrospective data. Also, the number of both parents and children/teenagers who returned the QoL questionnaire was modest, and we could not make comparisons between the patient subgroups.

5 | CONCLUSION

Parentally reported troublesome upper GI symptoms in early childhood did not associate with long-term GI morbidity at school age, excluding those with known conditions predisposing to GOR. However, the younger the child was, the more often parents reported current GI symptoms and decreased QoL. Dietary restrictions were not uncommon, warranting attention in the follow-up.

CONFLICT OF INTEREST

The authors have no relevant financial or non-financial interests to disclose.

CONSENT TO PARTICIPATE

A written informed consent was collected from all parents participating in the follow-up survey. Also, children who filled in the QoL

questionnaire provided their own informed consent. According to Finnish legislation, informed consent is not required for registry-based studies.

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