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Childhood Gastroesophageal Reflux Symptoms in Adult Patients

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ABSTRACT

Objectives: Gastroesophageal reflux (GER) and its esophageal (esophagitis, Barrett's esophagus) and extraesophageal (asthma, laryngeal disease) disease manifestations (GERD) are increasing common problems in children and adults. There are virtually no published longitudinal outcome studies that describe the natural history of childhood-onset GER throughout a person's lifetime. The aim of this study was to compare the frequency of recalled childhood reflux symptoms in adult patients currently with and without GER symptoms.

Methods: Four hundred adult patients were classified as refluxers (225 patients; 57%), nonrefluxers (154 patients; 38%), and those who claimed to not know if they had reflux (21 patients; 5%; excluded from analysis). Subjects were given a questionnaire asking them to recall childhood symptoms attributed to GER. Of the 225 refluxers, 141 (63%) recalled at least one childhood symptom, compared with 54 of the 154 nonrefluxers (35%) ($P < 0.001$).

Conclusions: Adult refluxers were more likely to recall having developed GER symptoms at an earlier age, beginning at infancy and developing statistically significant GER compared with nonrefluxers after age 11. Adults suffering from GER were far more likely than nonrefluxers to recall having experienced GER symptoms during childhood. Well-designed, population-based epidemiologic studies are needed to more accurately assess the extent of GER in the overall population and the extent of its impact on health care in the United States.
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Gastroesophageal reflux (GER) is a very common problem in adults, and its incidence appears to be increasing in the past decade (1–4). As many as 10% of Americans have daily heartburn, and 20% take over-the-counter antacids at least twice a week (5). Complications of GER, such as Barrett's esophagus, also appear to be increasing (6). A long-term sequelae of Barrett's esophagus and GER can be adenocarcinoma of the lower esophagus. The prevalence rate of adenocarcinoma of the esophagus are also increasing at an alarming rate (7–11). Recent data suggest that the length of time that a patient has heartburn is strongly associated with the development of esophageal adenocarcinoma (12).

Childhood GER is a common problem as well. Using the Pediatric Health Information System database and GER disease (GERD) as the single primary discharge diagnosis, a recent study has shown that the prevalence of hospital admissions for GER and GER-related sequelae has increased from less than 1% of all hospital admissions to 1.8% of hospital admission from 1995 to the year 2000 (13). Moreover, GERD represents 3.5% (approximately 65,000 discharges of 1.9 million admissions over the 5-year period) of all pediatric hospitalizations when the top three discharge diagnoses are evaluated (13). Additionally, based on history of GER symptoms and/or 24-hour pH-metry studies, GERD has been observed in up to 100% of 3-month-old infants, 40% of 6-month-old infants, and up to 20% of 12-month-old infants. In a small proportion of these children, symptoms never completely resolve (14–16). Many of the symptoms of reflux in childhood are different from the symptoms seen in adults (17–19). Children with GER may experience frequent regurgitation, irritability and inconsolable crying, nocturnal awakening associated with "painful" crying, respiratory symptoms, feeding refusal, and even failure to thrive (17,18,20–22). Complications of GER, such as Barrett's esophagus and esophageal adenocarcinoma, have been described in children as well (13,23,24–26). In addition to the increase in overall hospital admissions, the Pediatric Health Information System database has demonstrated that the prevalence of pediatric Barrett's esophagus increased from less than

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2% in 1997 to 3.8% in the first 6 months of 2000 (13). Whether the "true" incidence of Barrett's esophagus has actually increased or whether the increase in prevalence is a reflection of better endoscopic methodologies and increased surveillance needs to be determined.

Unfortunately, despite the indications of an overall increase in both GER and related esophageal and extra-esophageal manifestations (e.g., GERD-related asthma) in the United States, there are limited data available on the natural history of GERD in both children and adults (27). To date, there have been virtually no published longitudinal, prospective cohort outcome studies that describe what happens to children with symptomatic GER or its associated disease sequelae as they grow into adulthood. There have been numerous review articles on GER in children, but none describes long-term natural history, disease outcome, or predictors of long-term disease (17,18,20–22,28). Because it is clear that the long-term risk of untreated GER symptoms is associated with high morbidity and mortality, longitudinal, natural-history investigations are critically needed. It is our hypothesis that the majority of adults with symptomatic GER will have at one point in their childhood experienced GER-related symptoms. To test our hypothesis, we compared the prevalence of childhood reflux symptoms recalled by adult patients with and without current GER symptoms.

METHODS

Study subjects were adult patients recruited from two sources from September 1, 1999, to November 23, 1999: the outpatient general gastroenterology and medical clinic and the combined medical/surgical swallowing center at Emory University School of Medicine, The Emory Clinic. Patients were asked via questionnaire (Appendix) to recall symptoms related to GER that they might have experienced as infants and children. For the purpose of the questionnaire, infancy was defined as age birth to 18 months, and childhood was defined as age 19 months to 18 years. Patients were also asked to recall at what age the GER-related symptoms began. Patients initially categorized themselves as adult refluxers (study group; 61% women; approximate median age, 48 years) or nonrefluxers (control group; 55% women; approximate median age, 56 years). After obtaining informed consent, the questionnaire was administered to the subjects in the clinic waiting room by a study nurse blinded to the subject's diagnosis. The interviewer (M. F.) and the study nurse were available after receiving the completed questionnaire to provide answers to any questions. If any questions were unanswered, the interviewer would ask the subject for his/her response to complete the entire questionnaire.

The questionnaire was a one-page group of questions without skip questions which could be answered "yes," "no," or "can't answer". The questionnaire had been pilot-tested before the initial study enrollment for validation in the following categories: reproducibility of responses, ease of administration, recall differentiation between infant and childhood reflux symptoms, recall bias, and ease of differentiation between infant versus childhood reflux symptoms. Esophagogastroduodenoscopy (EGD) and/or 24-hour pH monitoring had been or was subsequently performed on a proportion (approximately 25%) of the GER study group to confirm diagnosis of GER. There was no paired, parallel EGD or pH-metry study assessment of the non-GER control patients for assessment of silent disease in this pilot study.

If available, one or more of the parents of the adult patients were asked about the subjects' recalled symptoms. Parents were available in approximately 10% of the overall study cohort and answered the same questionnaire about their child. Comparison between the subject's questionnaire responses and their parents' questionnaire responses was then performed and correlations obtained. Good correlation was observed between parental responses and those of the GER subjects, thereby providing us with some confidence as to the accuracy of the subject's own recall of his/her symptoms, and facilitating a decrease in recall bias. This pilot testing was performed to validate adult responses about childhood GERD symptoms. These data were then used to validate the use of the instrument in the adult subjects enrolled in the study. The study protocol was approved by the Emory University Human Investigations Committee. Comparisons between the groups were made using χ^2 analysis.

RESULTS

Four hundred adult patients completed the questionnaire at the time of their office visit. A total of 225 (56%) of the adults indicated that they had reflux, and 154 (38%) were classified as nonrefluxers; 21 patients (6%) claimed not to know whether they had reflux or not. Of the 25% of GER patients who had either EGD and/or pH-metry performed, GERD was confirmed by these clinical correlates in all. Of the 225 refluxers, 141 (63%) recalled at least one childhood symptom, compared with 54 of the 154 nonrefluxers (35%) ($P < 0.001$). Table 1 shows the overall specific responses for the comparison groups (GER vs. non-GER groups) to each question on the survey instrument. Differences between the two comparison groups were statistically significant for each of the survey instrument questions. Adult refluxers were more likely to recall having developed GER symptoms at an earlier age, usually beginning at infancy (Table 2). In

TABLE 1. *Responses to the questionnaire with corresponding* P *values*

	Refluxers (n = 225)	Nonrefluxers (n = 154)	*P**
Spit up as infant	23 (8.8%)	6 (3.8%)	0.02
Abdominal pain (epigastric pain)	48 (21.3%)	17 (11.0%)	0.009
Heart burn/chest pain	67 (29.7%)	14 (9.0%)	0.000001
Dysphagia	52 (23.1%)	20 (12.9%)	0.01
Underweight	47 (20.1%)	18 (11.6%)	0.02
Asthma	50 (22.2%)	9 (5.8%)	0.00002
Medication for GERD	31 (13.7%)	3 (1.9%)	0.00000005
Surgery for GERD	10 (4.4%)	0 (0%)	0.008

GERD, gastroesophageal reflux disease.

* $P < 0.05$ was considered statistically significant when comparing the two groups.

TABLE 2. *Number of patients recalling the age of onset of any gastroesophageal reflux symptom with cumulative* P *values*

Age (years)	Refluxers with early symptoms (n = 141)	Nonrefluxers with early symptoms (n = 54)	Cumulative *P* value
<1	12	7	0.74
1–3	9	4	0.45
3–6	7	4	0.41
6–10	20	7	0.08
11–16	28	11	0.009
>16	46	11	0.0000007
Unknown	18	10	

$P < 0.05$ was considered statistically significant when comparing the two groups.

addition, differences between childhood symptoms reported by the group of adults with current GER compared with nonrefluxing adults became statistically significant after age 11 (Table 2).

DISCUSSION

The prevalence rates of GER in both the pediatric and adult age groups appears to have increased over the latter part of the 1990s and into the 21st century. The reasons for this increased prevalence in GER and its related complications have not been clearly characterized. Cross-sectional and retrospective epidemiologic data suggest that adenocarcinoma of the distal esophagus as a long-term sequelae of GERD is also a significant health care problem both in the United States and around the world (8–11). Our initial study hypothesis was confirmed on all parameters examined in the two comparison groups by our survey instrument suggesting that childhood GER symptoms are common in adults who currently have reflux symptoms. In light of the worrisome changes in the epidemiology of GERD and its sequelae, our study suggests that there is a need for further investigations designed to define risk factors for the initial development of GERD. Additionally, our preliminary findings suggest that there is a critical need for further prospective study of the natural history of GERD in both the pediatric and adult age groups. Moreover, when considering the recently published investigations describing duration of GERD symptoms or heartburn as the single most important risk factors for the development of esophageal adenocarcinoma, the implications of our pilot study's findings are significant.

There were a number of limitations to this study. The survey instrument, although a simple questionnaire, was pilot tested and found to be reproducible in diverse populations and easy to understand. It was distributed directly to the patients attending a swallowing center for reflux symptoms. A potential patient response bias in the instrument's administration introduced by the selection of patients who were aware of the nature of the study objectives could not have been avoided. Although there are parallels between adult and pediatric GERD manifestations, many of the symptoms are different and therefore not likely to be mentioned because of bias. For example, most adults do not know that asthma, nocturnal awakening, feeding refusal, or failure to thrive are symptoms of childhood GER. In addition, having an experienced interviewer administer the questionnaire, rather than permitting self-administration by the subject, might have resulted in more accurate answers from study participants without conferring outright bias in the study participants. In addition, age-related recall bias may have affected the ability to accurately recall childhood symptoms, particularly in the older patients. Previous studies of recall bias have demonstrated that the longer the duration of time required for recall, the less accurate the answers. Validation of subject responses, albeit in a minor proportion of study participants, was achieved by the use of parent interviews. Interestingly, however, with respect to childhood symptoms or childhood experiences occurring in other disease entities, the more frequent and severe the "disease" and or symptoms that occurred during childhood, the more accurate the recall (29).

Our data provide preliminary evidence that childhood symptoms attributable to GER are commonly observed in adult refluxers. Not only did our working hypothesis hold up in this pilot study, but also the widely held notion that GERD is a life-long disease may be more close to the truth than we previously believed. We are currently initiating a prospective study using a similar questionnaire to compare adults with GERD confirmed by EGD- and pH-metry with two comparison groups (adult patients with other gastrointestinal disease [e.g., inflammatory bowel disease, irritable bowel syndrome] and healthy adult volunteers). Validated symptom scoring instruments that assess both presence and severity of GERD in children and adults, and that are applicable to both age groups, are critically needed, and studies are currently underway to develop such an instrument. The fact that the GER symptom instrument used in this study did not have validation against objective clinical correlates in the pediatric patient is another limitation of our study. However, the symptoms listed in the survey instrument and asked of the study participants are accepted as GER-related in the pediatric age groups in a variety of studies (30). Thus, based on the observations in our study, childhood GER does not always resolve spontaneously, and the disease may become clinically silent. We speculate that GER may persist throughout childhood, albeit not clinically apparent at times, into the adult age group, where it then becomes symptomatic again. Whether there are periods of peak incidence of symptoms and/or clinically evident disease in different age groups deserves attention in carefully designed multicenter cross-sectional or longitudinal studies.

In summary, when considering the apparent increase in the prevalence of GERD and GERD-related sequelae with its attendant morbidity, mortality, and health care impact, it is important to define preventable risk factors and initial age of acquisition of GERD, particularly in relation to symptom onset. In theory, if GERD actually begins in childhood, as is implied by our findings, and if there are indeed periods of symptom quiescence yet ongoing silent disease, more aggressive investigation and treatment of GERD in the pediatric age group may be warranted. Well-designed, population-based epidemiologic studies are needed to more accurately assess the extent of this problem and the overall health care impact of childhood-acquired GERD. From a public health perspective, despite the cost and logistical difficulty of conducting multicenter, longitudinal cohort studies, our study suggests a need to develop better diagnostic, intervention, and prevention strategies. There is a critical need for collaboration between adult and pediatric gastroenterologists who care for patients with GERD to extend our knowledge of GERD, assess the effects of treatment, and to evaluate the role of educational programs for parents of children with GERD in reducing the impact of this disease in the adult population.

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Appendix: Childhood GER Symptom Assessment Questionnaire

The Emory University Gastroenterology Department and the Division of Pediatric Gastroenterology and Nutrition is investigating the link between childhood and adult disease of the upper digestive tract. To help us with this research, we are asking you to complete the following short questionnaire. Most of the questions regard your childhood and may be difficult to remember—please answer them as accurately as you can. All answers will remain completely confidential.

Name:_____

I. Regarding your infancy (when you were less than 12 months old):

Were you ever told that you vomited or "spit up" frequently?
[1] yes [2] no [9] can't answer
Were you ever given medicine for heartburn or reflux?
[1] yes [2] no [9] can't answer
Did you ever have surgery to prevent vomiting or reflux?
[1] yes [2] no [9] can't answer

II. During any part of your childhood (birth to 18 years of age)?
Did you ever have abdominal (stomach) pain (particularly pain between the belly button and breast bone) occurring at least 2 times/week and lasting longer than three (3) months?
[1] yes [2] no [9] can't answer
Did you ever experience heartburn or chest pain occurring under the breast bone (sternum)?
[1] yes [2] no [9] can't answer
Did you ever have any problems with swallowing or have foods ever "stick" in your throat?
[1] yes [2] no [9] can't answer
Were you ever told that you were "underweight" or "small for your age," or did you see a doctor for "failure to thrive" or poor growth?
[1] yes [2] no [9] can't answer
Did you have asthma, wheezing, frequent cough, or, chronic hoarse voice, or use inhalers?
[1] yes [2] no [9] can't answer

III. If you answered "yes" to any of the above questions regarding your infancy or childhood, please check the age at which you first experienced any of the problems (or were told that you did):
less than 1 year old
1 to 3 years old
3 to 6 years old
6 to 10 years old
11 to 16 years old
older than 16 years old

IV. And finally, as an adult, are you now or have you ever been diagnosed or treated for reflux or heartburn?
[1] yes [2] no [9] can't answer

Thank you for your participation.