

Frequency of gastroesophageal reflux disease in adolescent girls with anorexia nervosa

Katarzyna Weterle-Smolińska¹, Marcin Dziekiewicz², Anna Liber²,
Marcin Banasiuk², Tomasz Wolańczyk¹, Urszula Szymańska¹,
Aleksandra Banaszekiewicz²

¹ Medical University of Warsaw, Department of Child Psychiatry

² Medical University of Warsaw, Department of Pediatric Gastroenterology and Nutrition

Summary

Aim. The aim of the study was to assess the incidence of gastroesophageal reflux disease (GERD) in young females with anorexia nervosa (AN).

Method. Participation in the study was proposed to young females with AN aged 12–18 who were hospitalized in the Department of Child Psychiatry, Medical University of Warsaw. Exclusion criteria were psychiatric disorders other than AN and treatment with prokinetic drugs and/or antacids (such as proton pump inhibitors or histamine receptor antagonists) in the last 2 weeks prior to the study. Patients were interviewed for gastrointestinal symptoms that can be related to GERD. Anthropometric measurements were obtained to assess the nutritional condition of the patients, and all of them were subjected to 24-hour pH-impedance monitoring. The pH-impedance recording was considered abnormal when the total number of reflux episodes exceeded 70 and/or the overall esophageal acid exposure time exceeded 6%.

Results. 23 female patients with AN were included in the study. They reported numerous symptoms, e.g., epigastric pain, nausea, vomiting, heartburn, chest pain, or excessive belching. However, only 2 of them (8.7%) were diagnosed with GERD on the basis of 24-hour pH-impedance monitoring. Both were suffering from a restrictive subtype of anorexia.

Conclusions. Even if numerous gastrointestinal symptoms indicative of GERD are reported by patients with AN, diagnosis of the disease in this group should not be based on symptoms, but it should be confirmed in an objective examination, preferably pH-impedance test.

Key words: anorexia nervosa, gastroesophageal reflux disease, child psychiatry

Introduction

Patients with anorexia nervosa (AN) very often report a wide range of gastrointestinal symptoms [1, 2]. Some of these symptoms can be a consequence of fasting or

rapid realimentation, e.g., intestinal motility disorders or superior mesenteric artery syndrome (a consequence of too sharp angle between the superior mesenteric artery and abdominal aorta, which causes pressure on duodenum and disrupts food transport) [3]. Certain symptoms can result from weight loss practices, e.g., frequent vomiting can lead to esophagitis, and abuse of laxatives can result in abdominal pain, diarrhea or constipation [4]. In addition, in the case of patients with AN, it cannot be excluded that reporting somatic symptoms is a justification for refraining from eating.

However, the symptoms presented above can also be indicative of a functional or organic gastrointestinal disease, such as gastroesophageal reflux disease (GERD). GERD symptoms are very common, as they occur even in 20% of the population [5]. GERD becomes a problem when the symptoms of gastroesophageal reflux become burdensome, disrupt everyday functioning or cause complications [6]. GERD symptoms include heartburn, belching, nausea, vomiting, burning, chest pain, and epigastric pain, which are a consequence of the damage to the lining of the esophagus caused by the gastric acid. Besides the above-mentioned symptoms, there is a wide range of extrasophageal symptoms of GERD, which result from the microaspiration of the gastric fluid into the respiratory tract. They occur less frequently than esophageal symptoms and include chronic dry cough, recurrent bronchitis, chronic hoarseness, or tooth enamel erosions. GERD, especially its aggravated esophageal symptoms, can lead to diminished appetite and weight loss. GERD in adolescents and adults can be diagnosed only on the basis of the reported symptoms; however, only if there are no alarm symptoms, such as weight loss. Therefore, in the case of patients with AN, the disease should not be diagnosed only on the basis of the reported symptoms. Occurrence of changes in the esophagus, which are a consequence of gastroesophageal reflux, can be objectively confirmed by gastroscopy. However, the best test to confirm the correlation between the occurrence of GERD symptoms and reflux episodes seems to be the 24-hour pH-impedance monitoring [7].

There have been only a few studies so far on patients with AN with gastrointestinal symptoms, including GERD. In addition, only single case studies are available that show GERD symptoms masking AN, or conversely, being a reason for AN misdiagnosis in patients. The aim of the study presented below was to assess the frequency of GERD in patients with AN on the basis of 24-hour pH-impedance test.

Material and method

A prospective study was conducted at the Department of Child Psychiatry, Medical University of Warsaw. Participation in the study was proposed to patients who met the following inclusion criteria:

- female;
- 12–18 years old;
- AN that was diagnosed on the basis of the ICD-10 criteria [8], and required hospitalization in a stationary psychiatric ward for children and adolescents;
- written consent of parents or guardians of the child patient to participate in the study, and the child's consent in the case of children ≥ 16 years of age.

The exclusion criteria were as follows:

- diagnosis of mental disorders other than AN;
- treatment with prokinetic drugs and/or antacids (e.g., proton pump inhibitors or histamine receptor antagonists) in the last 2 weeks prior to the study (in patients taking the above-mentioned drugs it was possible to stop treatment for 14 days, perform an examination and, if necessary, return to treatment).

All patients who had agreed to participate in the study were interviewed for demographic data and gastrointestinal symptoms that are characteristic of GERD, such as heartburn, belching, nausea, vomiting, chest pain, and epigastric pain.

Each patient was examined with regard to their nutritional status based on their body weight and height measurements. The measurements were taken in the morning, on an empty stomach and in underwear. BMI and body weight deficiency (controlled against the proper body weight) were calculated for each patient.

24-hour multichannel pH-impedance test (Sandhill Scientific Inc., Denver, CO, USA) was performed in all patients. In the test, probes with 6 impedance channels and a single pH electrode were used. The position of the probe was controlled using chest X-ray and modified, if necessary. The position was considered correct if the pH sensor was placed at 3 vertebrae above the diaphragm. Recording was made for at least 20 hours. The collected data were analyzed automatically, using the BioVIEW software, and manually to verify the automatic analysis. GER episodes were classified with regard to the pH value as acidic ($\text{pH} < 4$), weakly acidic ($4 < \text{pH} < 7$) and weakly alkaline ($\text{pH} > 7$). Due to the lack of well-developed norms for the interpretation of pH-impedance results in children, pH-impedance recording was considered abnormal when the total number of GER episodes exceeded 70 and/or the overall acid exposure time of the lining of the esophagus exceeded 6% [9].

An approval of the Bioethics Committee of the Medical University of Warsaw (KB/96/2009) was obtained in order to conduct the study.

Results

Participation in the study was proposed to 53 patients with AN who had met the inclusion criteria. Only 23 of whom (43.4%) gave their consent to participate in the study.

The study included 23 patients diagnosed with AN. Characteristics of the studied group including the diagnosis of GERD are presented in Table 1.

Table 1. Characteristics of the study group

	GERD (+) N = 2	GERD (-) N = 21	p
Age [months]	176.0	185.0	0.79
Body weight [kg]	33.0	39.0	0.33

table continued on the next page

Height [cm]	156.3	163	0.03
BMI [kg/m ²]	13.5	14.1	0.51
Type of anorexia nervosa [N (%)]			
restrictive	0	18 (85.7%)	<0.00001
bulimic	2 (100%)	3 (14.3%)	0.0005
The duration of anorexia nervosa symptoms until diagnosis [months.]	26.5	9.0	0.87
Gastrointestinal diseases in parents/siblings [N (%)]	1 (50%)	3 (14.3%)	0.2
Medication [N (%)]	2 (100%)	7 (33.3%)	0.065
Antidepressants	2 (100%)	6 (28.6%)	0.04
Neuroleptics	1 (50%)	2 (9.5%)	0.1

19/23 (82.6%) of the patients enrolled in the study reported symptoms that could be associated with GERD. They complained of epigastric pain, nausea, vomiting, heartburn, chest pain and, excessive belching. Table 2 shows the number of people with above-mentioned ailments including the diagnosis of GERD.

Table 2. Symptoms reported by the study participants

Symptom [N (%)]	Number of patients		p
	GERD (+) N = 2	GERD (-) N = 21	
Epigastric pain	1 (50%)	13 (61.9%)	0.27
Nausea	1 (50%)	9 (42.8%)	0.85
Vomiting	0	2 (9.5%)	0.65
Heartburn	0	8 (38.1%)	0.28
Chest pain	0	5 (23.8%)	0.44
Excessive belching	1 (50%)	8 (38.1%)	0.74

Although the patients reported numerous complaints, only 2 (8.7%) of them were diagnosed with GERD. The number of reflux episodes recorded in the 24-hour pH-impedance test conducted in these patients was higher than 70. One of the patients reported only epigastric pain, while the other one additionally experienced nausea and excessive belching. Both GERD patients presented a restrictive type of anorexia. One of the patients was not diagnosed with GERD on the basis of the determined criteria, although a significant number of weakly alkaline reflux episodes were recorded in the test. The patient complained of excessive belching.

In total, 653 episodes of gastroesophageal reflux (median 29, IQR 13–36) were reported. 235 (6; 2–16) were acidic, 398 (13; 8–23) – slightly acidic and 20 (0; 0–1) weakly alkaline. Acid exposure time in all studied patients was within the normal range.

Discussion

In the study presented above, GERD was diagnosed in almost every tenth patient with AN, using the 24-hour pH-impedance test. No such study has been conducted before in the pediatric population.

It is difficult to compare our result with the overall prevalence of GERD in healthy children. Due to the very wide spectrum of GERD symptoms, their low specificity and also due to the invasive nature of objective diagnostic tests (pH-metrics and pH-impedance), it has not been clearly determined yet. A recently published systematic review of the literature assessing the incidence of GERD in children has established that in the age group ≥ 10 years it ranges from 0.2% to 18.8%; the mean is 10.1% (95% CI 5.1–15.1) [5]. In six of the eight analyzed studies, only two symptoms of GERD were considered – heartburn and regurgitation.

Undoubtedly, GERD is one of the more common pathologies in the adult population. It is estimated that 8.8–25.9% of adults suffer from it in Europe [10]. According to our study, it seems that patients with AN are unlikely to develop GERD more often than the general population. Nor does it seem that the nature of reflux episodes is different from that of healthy adults [9]. The number of all reflux episodes (29 vs. 30) as well as weakly acidic (9 vs. 13) and weakly alkaline ones (0 vs. 0) was similar. There were some differences in the number of acidic episodes (6 vs. 18); it may be related to the reduced gastric secretion observed in malnourished children [11].

There are very few data describing GERD in adult patients with eating disorders and these are mainly case reports. This makes it impossible to compare the results of our study to the population of patients with AN. In their study, Winstead and Willard [4] determined that people with AN and previously diagnosed GERD (however, it was not stated on what basis) statistically more often reported the occurrence of gastroesophageal reflux disease symptoms than healthy individuals (2.4/week vs. 0.2/week, respectively; $p < 0.05$). Unfortunately, the cited study did not provide a definition of the symptom of GERD, and hence what is understood by this term is unknown. Benini et al. [12] estimated that over half of patients with AN reported symptoms of GERD: 15/23 – regurgitation and 14/23 – heartburn. However, again the diagnosis of GERD was not based on objective examination, but only on the symptoms reported by the patients themselves. In the population we analyzed, the frequency of reported symptoms was high. Only 4/23 (17.4%) of patients denied any gastrointestinal symptoms. The incidence of heartburn – 8/23 (34.8%) – was lower than in the study by Benini et al. [12]. Importantly, none of the patients diagnosed with GERD complained of heartburn or regurgitation. We also did not find statistically significant differences in terms of the occurrence of individual symptoms depending on the diagnosis of GERD. Until recently, heartburn was considered to be a symptom of GERD so typical that it allowed to make a diagnosis. Recently published criteria for recognizing functional gastrointestinal disorders, the so-called Rome Criteria, distinguished the functional heartburn, functional dysphagia, and functional chest pain. These pathologies are not related to excessive esophageal exposure to gastric contents and are quite often diagnosed in patients with mental disorders, including anxiety disorders and depression.

Moreover, diagnosis of GERD only on the basis of clinical symptoms is possible in the absence of the so-called alarm symptoms. Unfortunately, in the case of AN patients, there is always at least one alarm symptom, which is weight loss.

Symptoms such as heartburn, nausea, vomiting, epigastric pain, and dysphagia may also be signs of malnutrition in the course of AN. This hypothesis seems to be confirmed by the results of a study by Waldholtz and Andersen [13]. In 16 patients with AN who reported various gastrointestinal symptoms after admission to hospital, after 12 weeks of realimentation the frequency of symptoms, apart from belching, was reduced by more than 50%. It also seems that the time of intensive nutrition cannot be short. Heruc et al. [14] after 2 weeks of intensive realimentation of teenagers with JP did not observe a change in the frequency of reported gastrointestinal symptoms such as nausea or belching.

Patients with AN may also intentionally report gastrointestinal symptoms to justify their refusal to eat. Our patients reported symptoms frequently, and most of them (12/23) simultaneously reported ≥ 4 different symptoms. The search for justification for refusing food is common in patients with AN, especially during hospitalization, when weight gain and restoration of proper nutrition pattern is one of the first therapeutic goals. It has also been proven that the diet record prepared by the patients differs significantly from the objective record (according to the record of patients they eat more) [15].

Diagnosis of GERD only on the basis of reported clinical symptoms is often difficult for generally healthy people. For the reasons described above, it seems even more difficult and sometimes impossible for people with AN. In our opinion, in this group, GERD should be recognized only on the basis of the results of an objective test, preferably 24-hour pH-impedance.

Our study is the first to assess the prevalence of GERD in adolescents with diagnosed AN. Moreover, it was conducted in a relatively large group compared to other studies. GERD was diagnosed on the basis of 24-hour pH-impedance, a test that most objectively assesses the presence of reflux episodes. All studies conducted to date have used symptom questionnaires as a diagnostic tool.

The limitations of our study include a high percentage of patients who did not agree to participate in it. In all cases, this was dictated by the fear of discomfort associated with invasive diagnostic testing. The second most serious limitation of the study is the lack of a control group. Unfortunately, as mentioned above, pH-impedance is invasive. Therefore, carrying it out in a control group of healthy children is ethically questionable. For this reason, all scientific studies using pH-impedance and conducted in the pediatric population do not contain such a group. For this reason, normal values of 24-hour pH-impedance have not yet been established in the pediatric population. Furthermore, the large disproportion in the number of persons in the groups of patients suffering from GERD and those in whom it was excluded in the presence of a small general studied population means that the analysis of differences between the above mentioned in groups is difficult.

Conclusions

1. The incidence of GERD in girls with AN is not higher than in the general population despite frequently reported symptoms indicative of GERD.
2. The diagnosis of GERD in patients with AN cannot be based only on symptoms, but should be confirmed by an objective examination, preferably pH-impedance test.

References

1. Norris ML, Harrison ME, Isserlin L, Robinson A, Feder S, Sampson M. *Gastrointestinal complications associated with anorexia nervosa: A systematic review*. Int. J. Eat. Disord. 2016; 49(3): 216–237.
2. Szajnberg N. *Eating disorder and superior mesenteric artery syndrome*. J. Am. Acad. Child Adolesc. Psychiatry. 2001; 40(4): 388–389.
3. Sato Y, Fukudo S. *Gastrointestinal symptoms and disorders in patients with eating disorders*. Clin. J. Gastroenterol. 2015; 8(5): 255–263.
4. Winstead NS, Willard SG. *Gastrointestinal complaints in patients with eating disorders*. J. Clin. Gastroenterol. 2006; 40(8): 678–682.
5. Singendonk M, Goudswaard E, Langendam M, Wijk MV, Etten-Jamaludin FV, Benninga M et al. *Prevalence of gastroesophageal reflux disease symptoms in infants and children*. J. Pediatr. Gastroenterol. Nutr. 2019; 68(6): 811–817.
6. Rosen R, Vandenplas Y, Singendonk M, Cabana M, DiLorenzo C, Gottrand F et al. *Pediatric gastroesophageal reflux clinical practice guidelines*. J. Pediatr. Gastroenterol. Nutr. 2018; 66(3): 516–554.
7. Safe M, Cho J, Krishnan U. *Combined multichannel intraluminal impedance and pH measurement in detecting gastroesophageal reflux disease in children*. J. Pediatr. Gastroenterol. Nutr. 2016; 63(5): e98–e106.
8. Pużyński S, Wciórka J. *Klasyfikacja zaburzeń psychicznych i zaburzeń zachowania w ICD-10. Opisy kliniczne i wskazówki diagnostyczne*. Krakow: Vesalius; 2000.
9. Shay S, Tutuian R, Sifrim D, Vela M, Wise J, Balaji N et al. *Twenty-four hour ambulatory simultaneous impedance and pH monitoring: A multicenter report of normal values from 60 healthy volunteers*. Am. J. Gastroenterol. 2004; 99(6): 1037–1043.
10. El-Serag HB, Sweet S, Winchester CC, Dent J. *Update on the epidemiology of gastro-oesophageal reflux disease: A systematic review*. Gut. 2014; 63(6): 871–880.
11. Gilman RH, Partanen R, Brown KH, Spira WM, Khanam S, Greenberg B et al. *Decreased gastric acid secretion and bacterial colonization of the stomach in severely malnourished Bangladeshi children*. Gastroenterology. 1988; 94(6): 1308–1314.
12. Benini L, Todesco T, Frulloni L, Grave RD, Campagnola P, Agugiaro F et al. *Esophageal motility and symptoms in restricting and binge-eating/purging anorexia*. Dig. Liver Dis. 2010; 42(11): 767–772.
13. Waldholtz BD, Andersen AE. *Gastrointestinal symptoms in anorexia nervosa. A prospective study*. Gastroenterology. 1990; 98(6): 1415–1419.
14. Heruc GA, Little TJ, Kohn M, Madden S, Clarke S, Horowitz M et al. *Appetite perceptions, gastrointestinal symptoms, ghrelin, peptide YY and state anxiety are disturbed in adolescent*

females with anorexia nervosa and only partially restored with short-term refeeding. *Nutrients.* 2018; 11(1): 59.

15. Schebendach JE, Porter KJ, Wolper C, Walsh BT, Mayer LE. *Accuracy of self-reported energy intake in weight-restored patients with anorexia nervosa compared with obese and normal weight individuals.* *Int. J. Eat. Disord.* 2012; 45(4): 570–574.

Address: Marcin Dziekiewicz
Department of Pediatric Gastroenterology and Nutrition
Medical University of Warsaw,
02-091 Warszawa, Żwirki i Wigury Street 63A
e-mail: marcin.dziekiewicz@wum.edu.pl