

# Evaluation of 24-hour oesophageal pH monitoring in children with food allergy

## Ocena 24-godzinnego badania pH-metrycznego u dzieci z alergią pokarmową

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**Key words:** oesophageal pH monitoring, gastroesophageal reflux, allergy, children.

**Słowa kluczowe:** pH-metria przełyku, refluks żołądkowo-przełykowy, alergja, dzieci.

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### Abstract

**Introduction:** Gastroesophageal reflux (GER) and food allergy are conditions occurring most often in young children. Many authors emphasize the relationship between them.

**Aim:** To evaluate 24-h oesophageal pH monitoring in children with food allergy.

**Material and methods:** The retrospective analysis included 84 children with food allergy aged from 4 months to 24 months. The control group consisted of 15 children at the same age diagnosed with GER but without features of allergy. All children underwent 24-h oesophageal pH monitoring.

**Results:** Gastroesophageal reflux was diagnosed among children with allergy in 29 patients (34.5%). A gradual increase of the number and duration of reflux episodes in the period between meals compared to the postprandial period in both groups with GER was observed. The number of reflux episodes was higher in children with coexistent allergy. Analysis of graphic record of oesophageal pH monitoring revealed a primary reflux in 12 children with GER and allergy as well as in 9 children from the control group. In the remaining children from both groups the record showed features of secondary reflux, but the phases were not fully presented. The incidence of GER with features of secondary reflux was similar in both groups.

**Conclusions:** Twenty-four-hour oesophageal pH monitoring is helpful, but it cannot be the sole diagnostic criterion in the diagnosis of GER dependent on food allergy. Such a diagnosis should be based on the results of oesophageal pH monitoring as well as allergological and immunological tests.

### Streszczenie

**Wstęp:** Zarówno refluks żołądkowo-przełykowy (*gastroesophageal reflux* – GER), jak i alergja pokarmowa są chorobami najczęściej występującymi u najmłodszych dzieci. Wielu autorów podkreśla związki między nimi.

**Cel:** Ocena zapisu 24-godzinnego badania pH-metrycznego u dzieci z alergją pokarmową.

**Materiał i metody:** Retrospektywną analizą objęto 84 dzieci z alergją pokarmową w wieku od 4 miesięcy do 24 miesięcy. Grupę porównawczą stanowiło 15 dzieci w tym samym wieku z rozpoznanym GER, ale bez cech choroby alergicznej. U wszystkich dzieci wykonano 24-godzinne badanie pH-metryczne przełyku.

**Wyniki:** Wśród dzieci z alergją u 29 badanych (34,5%) wykazano obecność GER. Ocena analizowanych parametrów badania pH-metrycznego wykazała zarówno u dzieci z GER i alergją, jak i u dzieci z GER bez alergii stopniowe zwiększanie się liczby epizodów GER i czasu ich trwania w okresie międzyposiłkowym w stosunku do uzyskanych wartości w okresie poposiłkowym. Należy też zaznaczyć, że liczba epizodów GER była większa u dzieci ze współistniejącą alergją. Analiza zapisu graficznego badania pH-metrycznego przełyku wykazała GER pierwotny u 12 dzieci z GER i alergją oraz u 9 badanych z grupy porównawczej. U pozostałych dzieci z obu grup zapis wykazywał cechy GER wtórnego, ale nie był w pełni fazowy. Oceniana częstość występowania GER o cechach GER wtórnego była zbliżona w obu badanych grupach.

**Wnioski:** 24-godzinne badanie pH-metryczne przełyku jest pomocne, ale nie może być jedynym kryterium diagnostycznym w rozpoznawaniu GER zależnego od alergii pokarmowej. Powinno ono być oparte na wynikach zarówno badania pH-metrycznego przełyku, jak i badań alergologiczno-immunologicznych.

## Introduction

Food allergy is an important and frequent clinical problem, especially in the youngest children [1-3]. Similarly, gastroesophageal reflux disease is often seen in young children [4-6]. The relationships between these diseases have been described by many authors [7-14]. In our previous studies, the presence of gastroesophageal reflux was confirmed in 46.5% of children between 4 and 36 months of age with food allergy [15].

Reflux may be physiological, occurs rarely and is of short duration for example after exercise, less frequently during sleep. It is most commonly seen in newborns and infants born prematurely in the first few months of life due to immaturity of the anatomical-functional mechanisms protecting against backflow of gastric contents into the oesophagus [4, 10, 11, 16, 17]. Pathological reflux is characterized by increased frequency and intensity of episodes of acid regurgitation into the oesophagus and the occurrence of symptoms from other organs (gastroesophageal reflux disease). It occurs in children with an incidence of 1 : 100 to 1 : 300, according to different authors, and depends on age, coexisting diseases, and genetic, ethnic and racial factors [5, 7, 16, 18-20].

The pathomechanism of the formation of acid reflux may be primary, in which mechanisms of anti-reflux barrier are disturbed, or secondary, which is a clinical manifestation of other diseases, including food allergy [5, 7, 10, 11, 15, 16].

Twenty-four-hour oesophageal pH monitoring is widely regarded as the gold standard in diagnosis of gastroesophageal reflux. Evaluation of the recording allows differentiation of physiological from pathological reflux causing gastroesophageal reflux disease [6, 20-22]. However, it remains difficult to interpret the graphical recordings in order to determine the cause of pathological reflux. There is primary reflux resulting from insufficiency of the lower oesophageal sphincter and secondary reflux, which can be caused by various diseases including gastrointestinal disease, food allergy, metabolic diseases and neurological disorders. It can also occur after administration of certain drugs. It should be emphasized that the results of many authors concerning this problem are not fully unambiguous [9, 11, 12, 14, 15, 23, 24].

## Aim

The aim of the study was to analyse the record of 24-h oesophageal pH monitoring in children with food allergy.

## Material and methods

The retrospective analysis included 84 children with food allergy aged from 4 to 24 months. The control

group consisted of 15 children at the same age diagnosed with gastroesophageal reflux, but without any features of allergic disease. All examined children were treated in the 2<sup>nd</sup> Department of Paediatrics and Allergology of the Polish Mother's Memorial Hospital Research Institute in Lodz. Food allergy was diagnosed on the basis of the interview (clinical allergy symptoms and positive history of allergy in the family in some cases), positive food challenge test, and levels of serum concentration of allergen-specific antibodies (specific IgE) against cow's milk proteins. Concentrations  $\geq$  class 2 according to the 4-level classification of atopy confirmed IgE-mediated allergy [25].

All the children underwent 24-h oesophageal pH monitoring performed with Digitrapper Marc III (Synetics Medical, Sweden) using a probe with antimony electrodes calibrated prior to testing in a buffer solution at pH 7.01 and subsequently at pH 1.07.

The results were evaluated in accordance with the Sacre-Smits scale [26]. The parameters were assessed separately for the postprandial period (including the time of feeding with the next 2 h) and for the period between meals. The value of reflux ratio, number of reflux episodes, number of reflux episodes lasting longer than 5 min and duration of longest reflux were analysed.

The criteria of secondary reflux were fulfilled if the values of parameters mentioned above were higher in the period between meals than in the postprandial phase. Statistical analysis for the obtained data was applied.

## Results

The analysis of results revealed in 67 (79.8%) of 84 examined children with food allergy elevated levels of allergen-specific antibodies against proteins of cow's milk ( $\geq$  class 2). These children were diagnosed as IgE-dependent allergic while the remaining 17 children were classified as IgE-independent allergic individuals ( $p < 0.05$ ). Data from the medical interview showed positive family history for allergic disease in 61 children (72.6%).

The results of 24-h oesophageal pH monitoring evaluation confirmed gastroesophageal reflux disease (GERD) in 29 children (34.5%) with allergy to proteins of cow's milk. Among them there were 11 boys and 18 girls. The remaining 55 children with allergy were negative for reflux disease in 24-h pH-metry. In this group, unlike in children with coexisting gastroesophageal reflux, boys prevailed over girls (34/21). Similarly, the comparison group was also dominated by boys (9/6). The outcomes of evaluated parameters of 24-h oesophageal pH monitoring in children with and without food allergy are

**Table I.** Mean values of the analysed parameters of 24-h oesophageal pH monitoring in children in both examined groups**Tabela I.** Średnie wartości analizowanych parametrów 24-godzinnej pH-metrii przetyku u dzieci z obu badanych grup

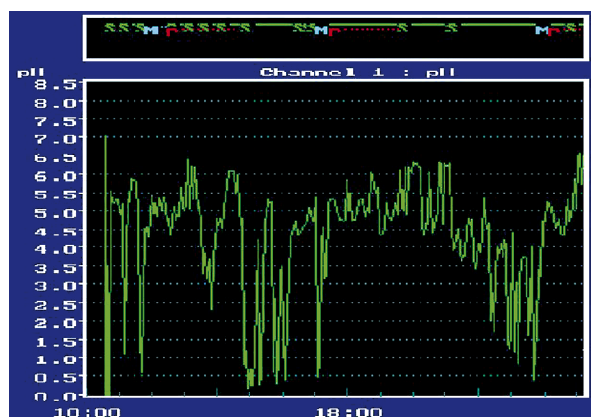
Parameter		Postprandial reflux		Reflux between meals	
		GER + allergy	GER	GER + allergy	GER
Index of reflux (%) ( $n < 5\%$ )	x	14.3	18.6	15.3	21.8
	SD	12.0	23.3	9.9	21.0
Number of reflux episodes ( $n < 50$ )	x	31.3	26.3	52.6	46.8
	SD	40.7	40.9	84.9	64.0
Number of reflux episodes lasting over 5 min ( $n < 9$ )	x	2.5	3.4	4.9	6.1
	SD	2.5	4.0	3.5	3.3
Duration of longest reflux episode ( $n < 9$ min)	x	22.6	28.3	40.4	47.4
	SD	23.2	29.5	46.3	32.2

shown in Table I. It was found that parameters such as number and duration of reflux episodes were significantly increased in the period between meals in relation to the postprandial period. However, the reflux ratio showed no significant difference between study periods, and the number of reflux episodes longer than 5 min was correct in both groups (study and control). It should be emphasized that the number of reflux episodes was higher for children with coexistent allergy. Mean values of evaluated parameters in children with allergy and children without allergic disease are shown in Table II. In addition, a detailed graphical analysis of the 24-h oesophageal pH monitoring recordings was performed, showing large difficulties of interpretation. These resulted from the fact that analysed results were not fully unambiguous. For each child the severity of reflux in

both analysed periods – postprandial and between meals – was compared. The analysis showed some differences. Among children with food allergy, in 12 children (41.4%) reflux was more intense in the period between meals and thus more similar to reflux secondary to allergy, while the remaining 17 children had reflux of primary character with higher intensity during the postprandial period. On the other hand, among children with reflux without allergy in 9 patients (60.0%) the results of oesophageal pH monitoring were characteristic for primary gastroesophageal reflux and in 6 patients (40.0%) for secondary reflux. Graphical records and examples are shown in Figures 1 and 2. The prevalence of primary and secondary reflux in both groups is shown in Figure 3. It shows that the frequency was similar in both groups.

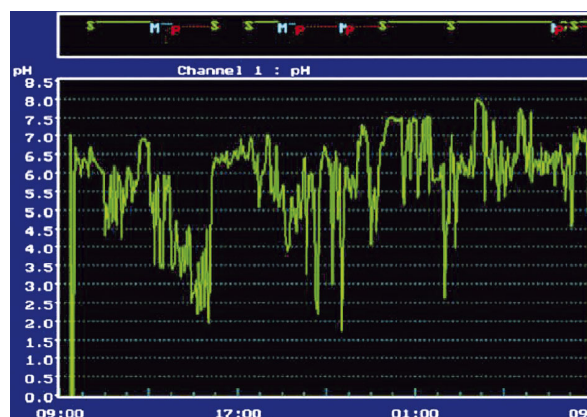
**Table II.** Mean values of the analysed parameters of 24-h oesophageal pH monitoring in examined children in accordance with type of reflux**Tabela II.** Średnie wartości analizowanych parametrów 24-godzinnej pH-metrii przetyku u dzieci z uwzględnieniem rodzaju refluksu

Parameter		Children with food allergy				Children without allergy			
		Primary ( $n = 17$ )		Secondary ( $n = 12$ )		Primary ( $n = 17$ )		Secondary ( $n = 12$ )	
		Post-prandial	Between meals	Post-prandial	Between meals	Post-prandial	Between meals	Post-prandial	Between meals
Index of reflux (%) ( $n < 5\%$ )	x	19.6	10.3	6.6	19.8	29.6	25.8	3.3	16.2
	SD	11.0	9.7	8.5	9.0	25.6	26.2	3.4	10.7
Number of reflux episodes ( $n < 50$ )	x	38.8	50.2	19.7	52.0	35.1	61.4	13.8	26.2
	SD	35.5	98.2	44.8	62.4	51.5	81.7	17.2	18.5
Number of reflux episodes lasting over 5 min ( $n < 9$ )	x	3.6	3.3	0.75	6.8	5.6	6.7	0.4	5.2
	SD	2.5	3.3	1.05	3.1	4.0	4.1	0.5	1.6
Duration of longest reflux episode ( $n < 9$ min)	x	27.0	23.3	15.3	61.3	44.9	50.6	5.2	43.0
	SD	20.2	23.9	25.5	60.3	28.5	35.9	5.3	29.6



**Fig. 1.** Graphical record of 24-h oesophageal pH monitoring – primary gastroesophageal reflux in a child with food allergy

**Ryc. 1.** Graficzny zapis 24-godzinnej pH-metrii przetyku – pierwotny GER u dziecka z alergią pokarmową



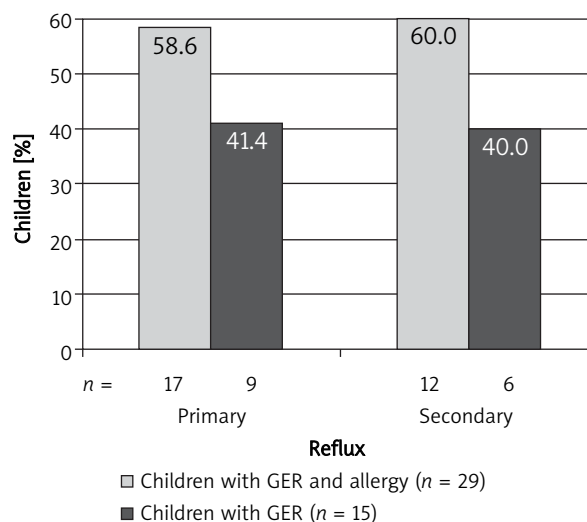
**Fig. 2.** Graphical record of 24-h oesophageal pH monitoring similar to the gastroesophageal reflux with features of secondary reflux, for example dependent on food allergy

**Ryc. 2.** Graficzny zapis 24-godzinnej pH-metrii przetyku zbliżony do GER z cechami GER wtórnego, np. zależnego od alergii pokarmowej

## Discussion

Food allergy in infants and young children most often is caused by IgE-dependent mechanisms [8, 10, 27]. Similarly, among our patients there was a high percentage of children (79.8%) with IgE-dependent allergy confirmed by a positive result of food challenge, and the presence of elevated serum levels of allergen-specific antibodies to cow's milk proteins. The allergy has great importance in the pathogenesis of gastroesophageal reflux, because food allergen adversely affects the mucous membrane of the oesophagus and promotes formation or increases the course of pathological reflux [8, 11, 28].

Many authors emphasize frequent and simultaneous occurrence of food allergy and gastroesophageal reflux [8-10, 12, 15, 17, 24]. Reflux may also be a clinical manifestation of allergy [10, 29]. Among our subjects about one third of children (34.5%) had both of these diseases. It should be noted that the incidence is similar to that observed by other authors, according to which it varies from 30% to 46% [10, 12, 15, 23, 24, 30]. The diagnosis of gastroesophageal reflux disease was confirmed by positive 24-h oesophageal pH monitoring, which is a reliable test in the diagnosis of gastroesophageal reflux [5, 6, 15, 21-24]. Analysis of the results showed differences in graphical recording of oesophageal pH monitoring in both the postprandial and between meals periods. It was found that there was a significantly higher number of reflux episodes in children with GER and allergy than in children with GER but without the aller-



**Fig. 3.** The percentage of children with secondary gastroesophageal reflux among subjects from both groups

**Ryc. 3.** Odsetek dzieci z wtórnym GER wśród badanych z obu grup

gy. These findings are compatible with the study results of Funkowicz *et al.* [9].

In the literature the need for differentiation between primary and secondary reflux is extensively emphasized, as it is important for the therapeutic procedure [9, 10, 12, 15, 30]. Therefore, like many other researchers we made an attempt of differential diagnosis on the basis of the graphical record of 24-h oesophageal pH monitoring. It should be noted, how-

ever, that this analysis is difficult and the observations of researchers are various. Cavatatio *et al.* [12] and Iacono *et al.* [13] observed that in children with allergy and gastroesophageal reflux the record varies depending on the cause. These authors found out that in primary reflux pH drops below four are irregular and of various duration. On the other hand, in secondary reflux there is a rapid increase of pH after the consumed meal with slow reduction to the next meal. Other investigators did not confirm these findings [9, 30-32]. In our study the record was typical of primary reflux in 17 children. However, in 12 subjects the recording with features of secondary reflux dependent on allergy aroused some doubts; it was intensified during the period between meals but this record was not fully phasic.

It seems therefore that this diversity of records should be analysed together with clinical symptoms and in allergic children with results of immunological and allergological tests, which is in accordance with the views of other authors [22, 23, 30].

Furthermore, demonstrating a similar prevalence of GER with features of secondary reflux in children with food allergy (12/29) and in the comparison group (6/15) indicates that the record of oesophageal pH monitoring cannot be the basis for the diagnosis of gastroesophageal reflux secondary to allergy to cow's milk. These observations are consistent with those of other authors [9, 10, 15, 30, 31].

## Conclusions

1. Twenty-four-hour oesophageal pH monitoring is helpful, but it cannot be the sole diagnostic criterion in the diagnosis of gastroesophageal reflux dependent on food allergy.
2. The diagnosis of gastroesophageal reflux dependent on allergy should be based on the results of oesophageal pH monitoring as well as allergological and immunologic tests.

## References

1. Sicherer S, Sampson H. Food allergy. *J Allergy Clin Immunol* 2006; 117 (2 Suppl Mini-Primer): 470-5.
2. Kamer B, Zielińska W, Raczyńska J, et al. The prevalence of allergic diseases in infants and young children in Lodz population. *Pediatr Pol* 1999; 74: 665-8.
3. Kaczmarek M, Cudowska B, Bandzul K, et al. The prevalence of food allergy in infants in North-East Poland. *Nowa Pediatria* 1999; 14: 26-28.
4. Nelson S, Chen E, Syniar G, et al. Prevalence of symptom of gastroesophageal reflux during infancy. A pediatric practice – based survey. *Pediatric Practice Research Group. Arch Pediatr Adolesc Med* 1997; 151: 569-72.
5. Iwańczak B, Iwańczak F. Clinical aspects of gastroesophageal reflux in children. *Pediatr Pol* 2004; 79: 495-501.
6. Kamer B, Chilarski A, Lange A, et al. Monitoring of the treatment of gastroesophageal reflux in infants and small children. *Przegl Pediatr* 1996; supl. 1/3: 227-32.
7. Salvatore S, Vandenplas Y. Gastroesophageal reflux and cow milk allergy: is there a link? *Pediatrics* 2002; 110: 972-84.
8. Janiszewska T, Czerwionka-Szaflarska M. IgE-dependent allergy – the intensification factor of gastroesophageal reflux in children and youth. *Med Wieku Rozw* 2003; 7: 211-22.
9. Funkowicz M, Wąsowska-Królikowska K, Tomaszewska M, et al. Role of pH-metry in diagnosing food allergy in young children. *Pediatr Pol* 2007; 82: 373-81.
10. Zielińska I, Czerwionka-Szaflarska M, Zawadzka-Gralec A, et al. Occurrence and clinical picture of food allergy in children and adolescents with acid gastroesophageal reflux. *Przegl Pediatr* 2009; 39: 92-8.
11. Semeniuk K, Tryniszewska E, Wasilewska J, et al. Food allergy – causal factor of gastroesophageal reflux in children. *Terapia* 1998; 5: 16-9.
12. Cavatatio F, Iacono G, Montalto G, et al. Gastroesophageal reflux associated with cow's milk allergy in infants: which diagnostic examinations are useful? *Am J Gastroenterol* 1996; 91: 1215-20.
13. Iacono G, Carroccio A, Cavataio F, et al. Gastroesophageal reflux and cow's milk allergy in infants: a prospective study. *J Allergy Clin Immunol* 1996; 97: 822-7.
14. Magazzu G, Scoglio R. Gastrointestinal manifestation of cow's milk allergy. *Ann Allergy Asthma Immunol* 2002; 89 (6 Suppl 1): 65-8.
15. Kamer B, Chilarski A, Lange A, et al. Gastroesophageal reflux in infants with food allergy. *Med Sci Monit* 2000; 6: 348-52.
16. Karczewska K, Jachimowicz M, Kalaciński W, et al. Clinical picture of gastroesophageal reflux in infants. *Przegl Pediatr* 1996; 26: 271-9.
17. Mowszet K, Iwańczak B, Matusiewicz K, et al. Gastroesophageal reflux in children with food allergy. *Nowa Pediatria* 2000; 21: 21-3.
18. Bielecki I, Mniszek J, Woś H. Laryngological aspects of gastroesophageal reflux disease in children. *Chir Pol* 2004; 1: 51-63.
19. Hegar B, Boediarso A, Firmansyah A, et al. Investigation of regurgitation and other symptoms of gastroesophageal reflux in Indonesian infants. *World J Gastroenterol* 2004; 10: 1795-7.
20. Dent J. Gastro-oesophageal reflux disease. *Digestion* 1998; 59: 433-45.
21. Nowak A, Marek T, Rydzewska G, et al. Polish Society of Gastroenterology guidelines: gastroesophageal reflux disease. *Gastroenterol Pol* 2005; 12: 313-9.
22. Kwiecień J, Fyderyk K. 24-hour esophageal pH-monitoring in children: methodology, indications, disadvantages. *Pediatr Współcz Gastroenterol Hepatol Żyw Dz* 2002; 4: 441-4.
23. Semeniuk J, Kaczmarek M. Acid gastroesophageal reflux and intensity of symptoms in children with gastroesophageal reflux disease. Comparison of primary gastroesophageal reflux and gastroesophageal reflux secondary to food allergy. *Adv Med Sci* 2008; 53: 293-9.
24. Cavataio F, Iacono G, Montalto G, et al. Clinical and pH-metric characteristic of gastro-oesophageal reflux secondary to cow's milk protein allergy. *Arch Dis Child* 1996; 75: 51-6.

25. Kjellman N, Johansson S, Roth A. Serum IgE levels in healthy children quantified by a sandwich technique. *Clin Allergy* 1976; 6: 51-6.
26. Vandenas Y, Sacre L. Continuous 24-hour esophageal pH monitoring in 285 asymptomatic infants 0-15 months old. *J Pediatr Gastroenterol Nutr* 1987; 6: 220-4.
27. Kaczmarek M. Allergy and civilization. KAW, Białystok 1990.
28. Hill D, Heine R, Cameron D, et al. Role of food protein intolerance in infants with persistent distress attributed to reflux esophagitis. *J Pediatr* 2000; 136: 641-7.
29. Wąsowska-Królikowska K, Plocek A, Toporowska-Kowalska E. Functional gastrointestinal disorders in food allergy in infants and young children. *Pediatr Współcz Gastroenterol Hepatol Żyw Dz* 2004; 6: 435-8.
30. Semeniuk J, Kaczmarek M. 24-hour esophageal pH monitoring in children with pathological acid gastroesophageal reflux: primary and secondary to food allergy. Part II. Intraesophageal pH values in proximal channel; preliminary study and control studies – after 1, 2, 4 and 9 years of clinical observation as well as dietary and pharmacological treatment. *Adv Med Sci* 2007; 52: 206-12.
31. Milocco C, Torre G, Ventura A, et al. Gastro-oesophageal reflux and cow's milk protein allergy. *Arch Dis Child* 1997; 77: 183-4.
32. Sampson H, Sicherer S, Birnbaum A. American Gastroenterological Association technical review on the evaluation of food allergy in gastrointestinal disorders. *Gastroenterology* 2001; 120: 1026-40.