

## CLINICAL MANIFESTATION OF GASTROESOPHAGEAL REFLUX DISEASE ASSOCIATED WITH AUTOIMMUNE THYROIDITIS IN YOUNG PERSONS

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### Abstract

**Background.** Gastroesophageal reflux disease (GERD) is one of the most common gastrointestinal disorders worldwide, with relevant impact on the quality of life and health care costs. The prevalence of GERD in Western Europe and North America is 30–40 % of the adult population, 10 % of them with daily heartburn as main symptom of GERD. The statistic data of GERD in Ukraine ranges from 11.1 % to 30 %. **Purpose.** To investigate the clinical features of gastroesophageal reflux disease which associated with autoimmune thyroiditis in young patients. **Subjects & Methods.** 165 patients have been studied. All patients were divided in two groups: first group consists of 120 patients with GERD associated with autoimmune thyroiditis (AIT), second group included had 45 patients with isolated GERD. Groups were matched in age ( $21.9 \pm 2.7$  and  $21.2 \pm 2.4$  years, respectively), sex (77.5 % and 75.5 % women, respectively), education and disease duration. **Results.** The main clinical symptom of GERD in patients with comorbid pathology and isolated GERD was heartburn, which was recorded in all cases, but its manifestations had different intensity, frequency, time of occurrence and duration. Patients of the group with the combined course of GERD and AIT significantly often noted the appearance of heartburn at night (65 %) in comparison with isolated GERD (31.1 %). Belching was observed in 62 patients (51.7 %) in the group with comorbid pathology and at 6 examined (13.3 %) in group with isolated GERD ( $p < 0.05$ ). **Conclusions.** Patients of the group with the combined course of GERD and AIT significantly more often had the night heartburn at – 65 % versus 31.1 % in the group with isolated GERD ( $p < 0.05$ ). Belching was observed in 52.5 % of patients with comorbid pathology and in 13.3 % of patients with isolated GERD ( $p < 0.05$ ). Assessment of other symptoms of GERD: epigastric discomfort, epigastric pain, dysphagia, nausea, vomiting, belching, satiety after meal, flatulence, hoarseness, cough did not have a significant difference between the groups, but there was a tendency to increase the incidence of symptoms in patients of the GERD group associated with AIT.

**Key words:** *gastroesophageal reflux disease, autoimmune thyroiditis, clinical characteristics.*

### Introduction

The beginning of the 21<sup>st</sup> century is characterized by growing prevalence of the main socially significant diseases of internal organs. Gastroesophageal reflux disease (GERD) is considered one of these diseases [1].

The 2014 review based on data of 16 studies of GERD showed that in North America

prevalence of GERD was 18.1–27.8 %, 23.0 % in South America, 8.8 %–25.9 % in Europe, 2.5–7.8 % in East Asia, 8.7–33.1 % in the Middle East, 11.6% in Australia; in the general population of the United Kingdom and the United States the incidence of GERD rate per 1000 population was approximately 5 persons [2].

According to more recent epidemiological data, the prevalence of GERD in Western Europe and North America is 30–40 % of the adult population, 10 % of them with daily heartburn as main symptom of GERD, but only 2 % of patients receive treatment [3]. Due to screening data of the endoscopic examination of the upper gastric tract in Japanese population esophagitis is detected

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in 16.5 % of all examined persons [4]. In Australia 11.3 % of patients visiting a general practitioner reveal GERD of chronic condition [5].

Recently endoscopic findings have shown an increase in erosive forms of GERD from 3.1 % to 16.0 % [6]. It was previously believed that the incidence of GERD increases with age, and its complications are usually found in patients older than 50 years. But epidemiological evidences suggest that now there is tendency to rising GERD rate in the young population [7,8]. In children, the prevalence of GERD, according to different observations is from 2–4 % to 8.7–49 % and the data is growing annually [9,10].

The prevalence of GERD in Ukraine ranges from 11.1–30% [11]. But clinicians emphasize that the given statistical results do not correspond with reality: such patients are much more, because almost a quarter of patients with complaints of GERD (usually heartburn) do not visit the doctors [12]. This is explained both to the young age of patients who first had the disease, and the lack of knowledge about the symptoms and signs of the disease [13]. The appearance of heartburn is often considered as a temporary unfavorable symptom of overeating or eating spicy food and the like ones. In this case, the disease for a long time remains uncontrolled, which contributes to its progression and the occurrence of complications.

Another unfavorable sign in the course of the disease is the addition of another nosological form, the pathogenic links of which intersect with the underlying disease. Among such diseases, the occurrence of which at a young age is quite common, is autoimmune thyroiditis (AIT). The prevalence of AIT in the world among the adult population is 20-30 % [14]. And there is data that confirms constant increase in incidence of AIT in young persons [15].

The provoking factors of AIT formation in young patients are: viral infection and its uncontrolled and inadequate treatment, acute or chronic diseases that preceded AIT and had a significant load on the immune system [16].

The combination of diseases of the internal organs is very typical for young persons who are in a specific environmental condition (students). A student's life consists of two parts – end-of-term exams and the period between exams. This has its equivalent of load: chronic stress and a period of complete relaxation. Such a distribution of time is one of the factors in the formation of the disease: during the exams "there is no time to get sick", and after they end – a long period of rest without attention to the health [17].

There were a few studies assessing the combined course of GERD and AIT but they mainly related to patients of older age groups. Currently, there are some studies about the role of thyroid hormones in the formation of motor and secretory disorders in young patients with GERD [18]. But main links of pathogenesis combination of GERD and AIT is unknown. This is the argument for further scientific research and clinical observations of young patients with a combination of these diseases. Determination of the phenotype of the clinical picture of GERD and AIT, the searching for common provoking factors play an important role in the clinic of internal diseases. Determination of the clinical features of GERD and AIT in this case very important for prevention the manifestation of complications.

## **2. Purposes, subjects and methods:**

**2.1. Purpose.** To investigate the clinical features of gastroesophageal reflux disease associated with autoimmune thyroiditis in young patients.

**2.2. Subjects & Methods.** The study involved 165 patients. All patients were divided in two groups: first group consisted of 120 patients with GERD associated with AIT, second group included 45 patients with isolated GERD. Groups were matched in age ( $21.9 \pm 2.7$  and  $21.2 \pm 2.4$  years, respectively), sex (77.5% and 75.5% women, respectively), education and disease duration.

Clinical examination of patients included: presentation, past and present history, physical examination, laboratory and instrumental methods of examination. The form of the disease was established taking into account visual changes in the mucous membrane of the esophagus (non-erosive or erosive) according to the video esophagogastroduodenoscopy data (Fuginon system) and recommendations of the Los Angeles Classification. Histomorphological studies of biopsy specimens have been performed for all patients.

The recommendations of the Montreal Consensus (2006), "Protocols for Patient Management ..." and the International Classification of Diseases of the 10th revision were used in establishing the diagnosis of GERD.

The presence of AIT was proved on the basis of palpatory examination of the thyroid gland, levels of antibodies to thyroperoxidase and thyroglobulin in blood serum, ultrasound data of the thyroid gland (apparatus Mindray DC-60 Exp).

The thyroid gland function was determined by the results of thyroid-stimulating hormone (TSH), free thyroxine (T4) and free triiodothyronine (T3). The diagnosis was proved with reference to the "Protocols of patient management ..." of the International Classification of Diseases of the 10<sup>th</sup> revision.

The study was conducted according to Medical-diagnostic standards and requirements for the ethical component of clinical trials (GCP, 1997). Patients were informed about the study, its purpose and possible results. Written consent to conduct the study was obtained from each patient who was involved, according to the recommendations of the ethical committees on biomedical research, the legislation of Ukraine on health, the Helsinki Declaration 2000 and European Society Directive 86/609 on the role of people in biomedical research.

Patients with diabetes mellitus, cardiovascular diseases, kidneys, oncological diseases of any localization, with mental illnesses, pregnant women and minors were not included in the study.

Standard statistics for the medical studies was used for the data analysis.

#### Conflict of interests.

There is no conflict of interests.

### 3. Results and discussion

The main clinical symptom of GERD in patients with comorbid pathology and isolated GERD was heartburn. In our study heartburn was recorded in all examined, but its manifestations had different intensity (*Figure 1*).

Patients with severe heartburn prevailed in both groups: 21 examined (17.5 %) in the first group and 4 (8.9 %) in the second group, but there were no significant differences between the groups.

Frequency, time of onset and duration of heartburn had the following distribution into groups (*Table 1*).

Daily incidence rate increased by 1.2 times and significantly frequent occurrence of this symptom at night in 78 patients (65 %) with a combination of GERD and AIT as compared to 14 persons (31.1 %) with isolated GERD.

The duration of the heartburn symptom was different: from 30–40 minutes to 2–3 hours and quite often its occurrence was stopped by taking medications in both groups.

Other symptoms of GERD included epigastric discomfort, epigastric pain, dysphagia, nausea, vomiting, belching, satiety after a meal, flatulence, hoarseness, cough (*Table 2*).

The prevalence of belching was significantly higher and occurred in 52.5 % (63 examined) of the group with GERD and AIT and in 6 patients (13.3 %) with isolated GERD. Among the other symptoms, there were no significant differences, but there was a tendency to increase the frequency of symptoms in patients with combined pathology.

The duration of the GERD history in the group of patients with combined course of diseases was as follows: the diagnosis was first established in 43 cases (35.8%); in other patients it ranged from 1 to 3 years. In the comparison group, the diagnosis of GERD was first established in 17 people (37.8%). The first visit to the doctor was from 7–8 months to 1.5 years after the onset of the first symptoms. According to the explanation of students the reasons of late visits to doctor were: either moderate clinical symptoms, "lack of time during the session" or a careless attitude toward oneself when clinical signs were considered temporary, associated with "the use of poor-quality food or drinks".

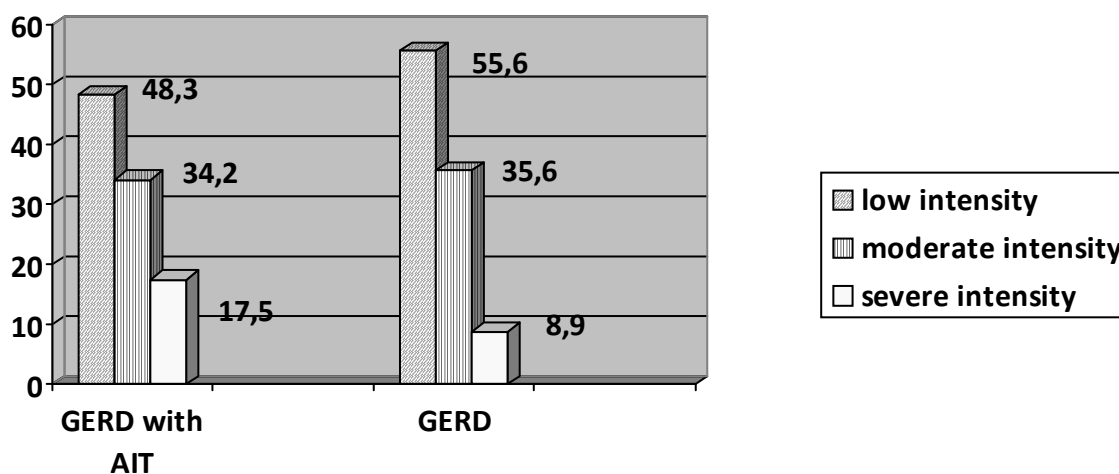


Fig. 1. Intensity of heartburn in examined patients with GERD and GERD associated with AIT, percentage

**Table 1**

*Frequency and time of occurrence of heartburn in patients with GERD and AIT and isolated GERD, abs. (%)*

Heartburn	GERD with AIT, n=120	GERD, n=45
Frequency of the heartburn (abs., %)		
Everyday	76 (63.3)	23 (51.1)
More than 2 times a week	44 (36.7)	22 (48.9)
Time of the episodes of the heartburn (abs., %)		
During the day	85 (70.8)	31 (68.9)
At night	78 (65.0)	14 (31.1)*

Note: \* – the difference is statistically significant between groups  $p < 0.05$ .

**Table 2**

*Frequency clinical symptoms of GERD occurrence in examined patients, abs. (%)*

Clinical sign	GERD with AIT, n=120	GERD, n=45
Epigastric discomfort	27 (22.5)	6 (3.3)
Epigastric pain	19 (15.8)	6 (13.3)
Dysphagia	8 (6.7)	2 (4.4)
Nausea	14 (11.7)	4 (8.9)
Vomiting	8 (6.7)	3 (6.7)
Belching	63 (52.5)	6 (13.3)*
Satiety after meal	41 (34.2)	11 (24.4)
Flatulence	47 (39.2)	14 (31.1)
Hoarseness	9 (7.5)	1 (2.2)
Cough	11 (9.2)	3 (6.7)

Note: \* – the difference is statistically significant between groups  $p < 0.05$ .

Among the all examined, 18 patients were smokers with smoking history from 7–10 cigarettes per day to half a pack. Smoking experience ranged from 6–7 to 3–4 years. The abuse of strong drinks was rejected by all groups, but they noted the use of low-alcohol drinks, such as beer. Also, almost all patients indicated frequent use of fizzy drinks.

Among the 165 students, 87 lived at home, the rest lived in a hostel or rented apartment. However, despite the different places of residence, there was practically no dietary and daily regime.

An additional survey of patients with GERD allowed to determine that almost all students did not adhere to the time of eating, volume and quality of food. Abuse of dry and spicy food, pastry, sweets were noted; and in most cases, the meal was taken on the go; between snacks there were different periods of time taking food and the first courses were practically not used. The feeling of hunger was often suppressed by smoking and drinking.

Nonconducted research of gastroesophageal reflux symptoms among Italian university students showed that 26.2% of the respondents had typical GERD symptoms occurring at least weekly [19].

According to statistic data GERD in combination with AIT is quite often registered in young patients. Such comorbidity contributes to unbalanced diet, stress, abuse of dry food and gas drinks, frequent viral infections and smoking [20].

Patients turned to the doctor in the delayed period, which can be explained by the "richness" of the life of young people and the lack of alertness for the occurrence of the disease.

The GERD on the background of autoimmune inflammation concerns with the worsening and increasing in the frequency of individual clinical symptoms (intensity of heartburn and its registration at night, belching), which can be considered as unfavorable factors for the progression of the disease and its chronicity.

Comparison of the clinical symptoms of patients with isolated GERD and GERD associated with AIT in our study revealed that all patients had heartburn with different intensity in our study. Low intensity of heartburn was registered in 17.5 % cases, moderate in 34.2 % and severe intensity in 48.3 %. Research that was conducted among medical students from southern India has shown that heartburn with low intensity was in 58.6 % of examined, 38.6 % had moderate and 2.8 % had severe GERD [21].

Night heartburn was registered in 78 patients of the first group and in 14 examined of the second group GERD ( $p < 0.05$ ). Belching occurred significantly more often in the group with comorbid pathology (63 patients versus 6 persons in group with isolated GERD).

I.V. Baranov and T.V. Maikova showed in their study the relationship between the level of thyroid hormones and the severity of the atrophy and inflammatory changes in the mucous membrane of the esophagus. However, the authors did not investigate the features of secretion in this group of patients, as well as the clinical course of GERD, depending on the presence of AIT [22].

V.T. Ivashkin and I.V. Maev analyzed in detail the characteristics of GERD therapy taking into account the clinical picture of the disease, the characteristics of the secretion and morphological state of the GERD mucosa. However, the features of the course of GERD in the presence of concomitant thyroid pathology during the

course of GERD and the formation of motor-secretory disorders were not studied [23].

Considering the above, it can be speculated that associated AIT produced a negative impact on the course of GERD, but pathogenic relationship between these diseases are not well defined and requires further research.

#### 4. Conclusions

1. Patients of the group with the combined course of GERD and AIT significantly more often had night heartburn in 65% versus 31.1% in the group with isolated GERD ( $p < 0.05$ ).

2. Belching was observed in 52.5% of patients with comorbid pathology and in 13.3% of patients with isolated GERD ( $p < 0.05$ ).

3. Assessment of other symptoms of GERD: epigastric discomfort, epigastric pain, dysphagia, nausea, vomiting, belching, satiety after meal, flatulence, hoarseness, cough did not have a significant difference between the groups, but there was a tendency to increase the incidence of symptoms in patients of the GERD group associated with AIT.

#### References

1. Fakhre Yaseri H. (2017). Gender is a risk factor in patients with gastroesophageal reflux disease. *Medical journal of the Islamic Republic of Iran*, 31, 58. doi:10.14196/mjiri.31.58
2. El-Serag HB, Sweet S, Winchester CC, Dent J. (2014). Update on the epidemiology of gastro-oesophageal reflux disease: A systematic review Article. *Literature Review in Gut* 63(6):871–880 doi: 10.1136/gutjnl-2012-304269.
3. Gyawali, C. P., Kahrilas, P. J., Savarino, E., Zerbib, F., Mion, F., Smout, A., ... Roman, S. (2018). Modern diagnosis of GERD: the Lyon Consensus. *Gut*, 67(7), 1351–1362. doi:10.1136/gutjnl-2017-314722
4. Klenzak, S., Danelisen, I., Brannan, G. D., Holland, M. A., & van Tilburg, M. A. (2018). Management of gastroesophageal reflux disease: Patient and physician communication challenges and shared decision making. *World journal of clinical cases*, 6 (15), 892–900. doi:10.12998/wjcc.v6.i15.892
5. Harrison C, Henderson J, Miller G, Britt H. (2017). The prevalence of diagnosed chronic conditions and multimorbidity in Australia: a method for estimating population prevalence from general practice patient encounter data. *PLoS One*. 12(3):e0172935. doi: 10.1371/journal.pone.0172935.
6. Ye, B. X., Jiang, L. Q., Lin, L., Wang, Y., & Wang, M. (2017). Reflux episodes and esophageal impedance levels in patients with typical and atypical symptoms of gastroesophageal reflux disease. *Medicine*, 96(37), 79–78. doi:10.1097/MD.00000000000007978
7. Yamasaki, T., Hemond, C., Eisa, M., Ganocy, S., & Fass, R. (2018). The Changing Epidemiology of Gastroesophageal Reflux Disease: Are Patients Getting Younger?. *Journal of neurogastroenterology and motility*, 24(4), 559–569. doi:10.5056/jnm18140
8. Galos F, Boboc C, Balgradean M (2016). Gas Reflux in Children with Normal Acid Exposure of the Oesofagus. *Maedica (Buchar)*, Vol. 11, Issue 4. – P. 345–348
9. Eiko Okimoto, Norihisa Ishimura, Yoshiya Morito, Hironobu Mikami, Shino Shimura, Goichi Uno, Yuji Tamagawa, Masahito Aimi, Naoki Oshima, Kousaku Kawashima, et al. (2015). Prevalence of gastroesophageal reflux disease in children, adults, and elderly in the same community. *J Gastroenterol Hepatol.*, 30 (7): 1140–1146. doi: 10.1111/jgh.12899
10. Leung, A. K., & Hon, K. L. (2019). Gastroesophageal reflux in children: an updated review. *Drugs in context*, 8, 212591. doi:10.7573/dic.212591
11. Fadiencko, H.D., Halchinska, V.Yu., Kushnir, I.E. (2016). Violation of the functional state of the endothelium and its role in the pathogenesis of gastroesophageal reflux disease combined with coronary heart disease. *Modern Gastroenterology*, 5 (91), 9–14.

12. Monroy, M., Ruiz, M. A., Rejas, J., & Soto, J. (2018). Mapping of the Gastrointestinal Short Form Questionnaire (GSF-Q) into EQ-5D-3L and SF-6D in patients with gastroesophageal reflux disease. *Health and quality of life outcomes*, 16(1), 177. doi:10.1186/s12955-018-1003-y
13. Ebrahimi-Mameghani, M., Sabour, S., Khoshbaten, M., Arefhosseini, S. R., & Saghafi-Asl, M. (2017). Total diet, individual meals, and their association with gastroesophageal reflux disease. *Health promotion perspectives*, 7(3), 155–162. doi:10.15171/hpp.2017.28
14. Kiel S, Ittermann T, V?lzke H, Chenot JF, Angelow A (2019). Prevalence of thyroid abnormality: a comparison of ambulatory claims data with data from a population-based study. *Bundesgesundheitsblatt Gesundheitsforschung Gesundheitsschutz*. 62(8):1004–1012. doi: 10.1007/s00103-019-02983-1.
15. Pyzik, A., Grywalska, E., Matyjaszek-Matuszek, B., & Roli?ski, J. (2015). Immune disorders in Hashimoto's thyroiditis: what do we know so far?. *Journal of immunology research*, 2015, 979167. doi:10.1155/2015/979167
16. Bliddal, S., Nielsen, C. H., & Feldt-Rasmussen, U. (2017). Recent advances in understanding autoimmune thyroid disease: the tallest tree in the forest of polyautoimmunity. *F1000Research*, 6, 1776. doi:10.12688/f1000research.11535.1
17. Alrashed, A. A., Aljammaz, K. I., Pathan, A., Mandili, A. A., Almatrafi, S. A., Almotire, M. H., & Bahkali, S. M. (2019). Prevalence and risk factors of gastroesophageal reflux disease among Shaqra University students, Saudi Arabia. *Journal of family medicine and primary care*, 8(2), 462–467. doi:10.4103/jfmpe.jfmpe\_443\_18
18. Cellini, M., Santaguida, M. G., Virili, C., Capriello, S., Brusca, N., Gargano, L., & Centanni, M. (2017). Hashimoto's Thyroiditis and Autoimmune Gastritis. *Frontiers in endocrinology*, 8, 92. doi:10.3389/fendo.2017.00092
19. Martinucci, I., Natilli, M., Lorenzoni, V., Pappalardo, L., Monreale, A., Turchetti, G., ... de Bortoli, N. (2018). Gastroesophageal reflux symptoms among Italian university students: epidemiology and dietary correlates using automatically recorded transactions. *BMC gastroenterology*, 18(1), 116. doi:10.1186/s12876-018-0832-9
20. Rajaie S, Ebrahimpour-Koujan S, Hassanzadeh Keshteli A, Esmailzadeh A, Saneei P, Daghighzadeh, Feinle-Bisset, Adibi. (2019). Spicy Food Consumption and Risk of Uninvestigated Heartburn in Isfahani Adults. *Dig Dis*. 30:1–10. doi: 10.1159/000502542
21. Sharma, A., Sharma, P. K., & Puri, P. (2018). Prevalence and the risk factors of gastro-esophageal reflux disease in medical students. *Medical journal, Armed Forces India*, 74(3), 250–254. doi:10.1016/j.mjafi.2017.08.005
22. Baranov I.V., Maykova T.V. (2010). Endoscopic characteristics of the esophagus, stomach and duodenum in patients with gastroesophageal reflux disease in combination with primary hypothyroidism. *News of Medicine and Pharmacy. Gastroenterology (thematic number)*, 337.
23. Ivashkin V.T., Maev I.V., Trukhmanov A.S. et al. (2017) Clinical recommendations of the Russian Gastroenterological Association for the diagnosis and treatment of gastroesophageal reflux disease. *Ros. journal gastroenterol., hepatol. and coloproctol*, 27(4), 75–95. doi: 10.22416/1382-4376-2017-27-4-75-95.

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