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# Evaluation of the prevalence of glucose metabolism disorders in patients with dyspepsia

## ABSTRACT

**Introduction.** As estimated by IDF, by 2045 there will be about 628 million of people living with diabetes, of which 87–91% will have type 2 diabetes. Therefore, early diagnosis of diabetes is very important, and currently only 4–50% of cases are diagnosed early enough. The aim of the study was to establish whether patients with dyspepsia may potentially be a group at high risk of developing diabetes in which screening for glucose metabolism disorders would be particularly important. **Material and methods.** The study included 59 women (65.5%) and 31 men (34.5%), with a mean age of 36 years, hospitalized in order to perform gastroscopy due to symptoms of dyspepsia. All patients were apparently healthy, without the history of cardiovascular diseases or diabetes, and were non-smokers. The patients were subjected to laboratory tests (random blood glucose, oral glucose tolerance test [OGTT], lipid profile, C-reactive protein level), gastroscopy and a rapid urease test for detection of active *Helicobacter pylori* infection. Body mass index (BMI) was also calculated. Subjects with abnormal results of the oral glucose tolerance test (OGTT) were assigned to the group with glucose metabolism disorders and the remaining subjects — to the group without glucose metabolism disorders.

Statistical analysis of the obtained research results was carried out using the Statistica 7.0 PL software.

**Results.** The subjects were divided into two subgroups based on the result of the oral glucose tolerance test, adopting the principles of diagnosing carbohydrate metabolism disorders according to the Diabetes Poland. The group with glucose metabolism disorders included 33 patients (36.5%): 5 subjects (5.5%) with impaired fasting glucose, 20 patients (22%) with impaired glucose tolerance and 8 patients (9%) with diabetes. The remaining 57 (63.5%) patients had normal results of OGTT and were assigned to the group without glucose metabolism disorders. The mean BMI in the whole examined population was 26.7 kg/m<sup>2</sup>. Patients with glucose metabolism disorders (GMD) had a significantly higher BMI (31.1 kg/m<sup>2</sup>). The levels of total cholesterol, LDL cholesterol and TG were higher in patients with GMD; however, the difference was not statistically significant. Random blood glucose values were significantly higher in the group with GDM, but no patient had random blood glucose  $\geq$  200 mg/dL. The HbA<sub>1c</sub> value was significantly higher in the GMD group. Also, the C-reactive protein (CRP) level was significantly higher in the group of patients with GMD than in the group of healthy subjects. All patients underwent gastroscopy and abnormal results were found in 41 patients (45.5% of total study population) — in 67% in the group with GMD and 33% in the group without GDM. The most frequent pathology was *Helicobacter pylori* infection (25.5%). This infection was more prevalent in the group with GDM (45%) than in the group without GDM (14%). In addition, gastritis, gastric cancer, gastro-esophageal reflux, hiatal hernia, and gastric polyps were found, without significant differences between the subgroups.

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**Conclusions.** Over 1/3 of the subjects with dyspepsia had prediabetes or diabetes; therefore, it seems that this group of patients should be screened for glucose metabolism disorders. High prevalence of GMD among patients with dyspepsia indicates potential benefits of performing OGTT in this group of patients. Gastrointestinal symptoms may be an early manifestation of glucose metabolism disorders. There is a correlation between *Helicobacter pylori* infection and the presence of glucose metabolism disorders. (Clin Diabetol 2018; 7, 6: 253–258)

**Key words:** type 2 diabetes, glucose metabolism disorders, dyspepsia

## Introduction

Type 2 diabetes is considered as a social disease and its prevalence is constantly growing. It is estimated that in 2045 there will be about 628 million people with diabetes. Currently, only 40–50% of cases are properly diagnosed, which enables the implementation of effective treatment. In the remaining 50–60% diabetes is undiagnosed, which — despite the oligosymptomatic course — leads to gradual development of complications. Due to the often asymptomatic course of the early stages of type 2 diabetes, screening is of key importance for early diagnosis, especially in groups of patients at increased risk of carbohydrate disorders.

Dyspeptic symptoms are very common. Recent studies show that dyspepsia is more prevalent in patients with diabetes than in non-diabetic subjects. Therefore, it has been hypothesized that the presence of dyspeptic symptoms could be useful in identifying a group of patients with higher risk of asymptomatic glucose metabolism disorders, including prediabetes. Screening these patients for glucose metabolism disorders may result in early diagnosis and consequently early implementation of treatment, thus protecting patients from silent complications of diabetes and even diabetes itself.

The aim of the study was to establish whether patients with dyspepsia may potentially be a group at high risk of developing diabetes in which screening for glucose metabolism disorders would be particularly important.

## Material and methods

The study included 90 people, 59 women (65.5%) and 31 men (34.5%), with an mean age of 36 years, hospitalized in the 2nd Department of Cardiology and Internal Diseases of the University Clinical Hospital in Olsztyn in order to perform gastroscopy due to symp-

toms of dyspepsia. Included in the study were apparently healthy patients, without the history of cardiovascular diseases or diabetes, and were non-smokers.

Dyspepsia was defined as the presence of at least 1 of the following symptoms: epigastric pain, feeling of fullness, epigastric discomfort, and eructation [1]. The examined patients had the symptoms of dyspepsia for at least 3 months. All patients underwent physical examination including blood pressure measurement and the calculation of the body mass index (BMI), according to the Quetelet formula, where  $BMI = \text{body weight [kg]} / \text{height [m]}^2$ .

Following laboratory tests were performed in each patient:

- glycemic profile:
  - glycated hemoglobin ( $HbA_{1c}$ ),
  - blood glucose at admission (random),
  - blood glucose on fasting state and 2 hours after administration of 75 g glucose (oral glucose tolerance test, OGTT). On the basis of OGTT, the following glucose metabolism disorders (GMD) were diagnosed:
    - 1) impaired fasting glucose (IFG),
    - 2) impaired glucose tolerance (IGT),
    - 3) diabetes mellitus (DM),
- lipid profile: total cholesterol, LDL cholesterol, HDL cholesterol, triglycerides;
- C-reactive protein (CRP).

All laboratory tests were performed using standard methods.

Gastroscopy was carried out using Olympus GIF-Q165 and GIF-Q180 apparatus, by a qualified endoscopist, certified in panendoscopy by the Polish Society of Gastroenterology.

A rapid urease test was used to diagnose *Helicobacter pylori* infection.

The study was approved by the Bioethical Committee of the Warmia and Mazury Regional Medical Chamber in Olsztyn on 4th December 2012. It included analysis of results of standard diagnostic test and voluntary and anonymous surveys.

## Statistical analysis

Statistical analysis of the test results was carried out using the Statistica 7.0 PL software. To verify hypotheses about the existence or absence of relationship between categorized variables, the Pearson 2 test and 2 NW test (the highest reliability) were used. To compare the mean values of measurable variables, the Student's t-test or the nonparametric Mann-Whitney U test were used (for comparisons between two groups). The Chi-square test was used to compare the qualitative variables using cross-tabulation table. The Schapiro-Wilk test was used

to analyze measurable variables that were non-normally distributed. 95% confidence intervals (95% CI) were determined for the analyzed values. P-values < 0.05 were considered as statistically significant.

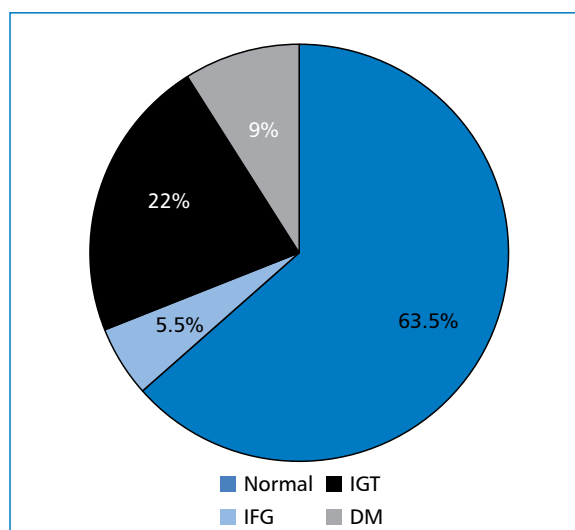
## Results

The study included 90 people with a mean age of  $36.1 \pm 12.5$  years (59 women [65.5%] and 31 men [34.5%], hospitalized in the 2nd Department of Cardiology and Internal Diseases of the University Clinical Hospital in Olsztyn due to dyspepsia.

The subjects were divided into two subgroups based on the result of the oral glucose tolerance test (OGTT), adopting the principles of diagnosing carbohydrate metabolism disorders according to the Diabetes Poland. The group with glucose metabolism disorders included 33 patients (36.5%): 5 subjects (5.5%) with impaired fasting glucose, 20 patients (22%) with impaired glucose tolerance and 8 patients (9%) with diabetes. The remaining 57 (63.5%) patients had normal results of OGTT and were assigned to the group without glucose metabolism disorders (Figure 1).

The mean BMI in the whole examined population was  $26.7 \text{ kg/m}^2$ . Patients with glucose metabolism disorders (GMD) had a significantly higher BMI ( $31.1 \text{ kg/m}^2$ ) compared to those without GMD ( $24.1 \text{ kg/m}^2$ );  $p = 0.007$ . The levels of total cholesterol, LDL cholesterol and TG were higher in patients with GDM; however, the difference was not statistically significant (Table 1).

Random blood glucose values were significantly higher in the group with GDM than in healthy subjects ( $86.9 \text{ mg/dL}$  vs.  $93.03 \text{ mg/dL}$ , respectively;  $p < 0.017$ ). No patient had random blood glucose  $\geq 200 \text{ mg/dL}$ .



**Figure 1.** The prevalence of glucose metabolism disorders in patients with dyspepsia. According to the Diabetes Poland guidelines: **random blood glucose**  $\geq 200 \text{ mg/dL}$  ( $\geq 11.1 \text{ mmol/L}$ ), measured at the time when symptoms of hyperglycemia are presented — diabetes mellitus (DM); **fasting blood glucose**:  $70\text{--}99 \text{ mg/dL}$  — normal fasting blood glucose,  $100\text{--}125 \text{ mg/dL}$  — impaired fasting glucose (IFG),  $\geq 126 \text{ mg/dL}$  on two occasions — DM; **blood glucose at 120 minutes of oral glucose tolerance test (OGTT)**:  $< 140 \text{ mg/dL}$  — normal glucose tolerance (NGT),  $140\text{--}199 \text{ mg/dL}$  — impaired glucose tolerance (IGT),  $\geq 200 \text{ mg/dL}$  ( $11.1 \text{ mmol/l}$ ) — DM [20]. IFG — impaired fasting glucose; IGT — impaired glucose tolerance; DM — diabetes mellitus

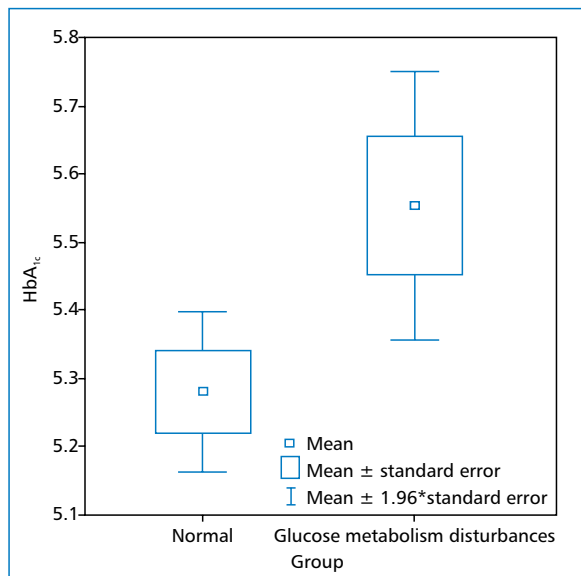
The  $\text{HbA}_{1c}$  value was significantly ( $p < 0.024$ ) higher in the GMD group and amounted to 5.5% (Figure 2).

In the group of patients with GMD C-reactive protein (CRP) level was  $1.3 \text{ mg/L}$  — significantly ( $p < 0.003$ ) higher than in the group without GDM (Figure 3).

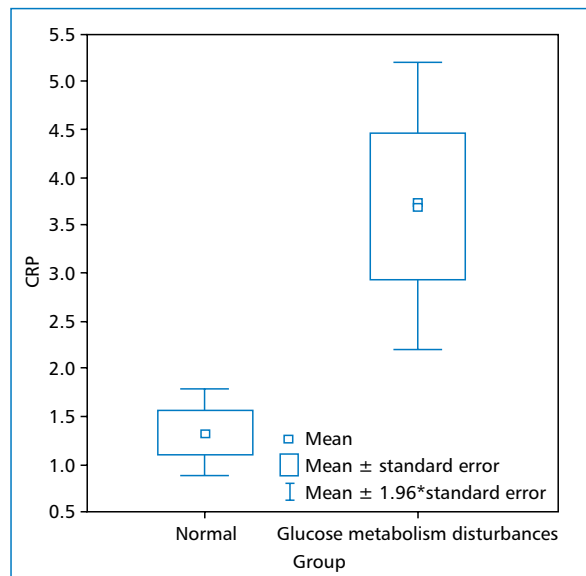
**Table 1.** General characteristics of the examined group according to presence of absence (healthy subjects) of glucose metabolism disorders (GMD)

Parameter	Study groups n (%)			p
	Total 90 (100%)	Healthy subjects 57 (63%)	GMD 33 (37%)	
Age [years, SD]	$36.1 \pm 12.5$	$35.2 \pm 12.5$	$37.7 \pm 12.6$	0.367
BMI [ $\text{kg/m}^2$ ] [SD]	$26.7 \pm 8.3$	$24.1 \pm 4.6$	$31.1 \pm 11.1$	0.007
Total cholesterol [mg/dl] [SD]	$189.1 \pm 42.0$	$184.2 \pm 42.0$	$197.4 \pm 41.3$	0.154
LDL cholesterol [mg/dl] [SD]	$107.9 \pm 32.1$	$105.9 \pm 31.3$	$111.3 \pm 33.7$	0.445
HDL cholesterol [mg/dl] [SD]	$55.0 \pm 15.4$	$55.7 \pm 14.3$	$53.9 \pm 17.4$	0.59
Triglycerides [mg/dl] [SD]	$109.8 \pm 57.9$	$97.6 \pm 43.1$	$130.7 \pm 73.3$	0.069
Random glycemia [mg/dl] [SD]	$89.2 \pm 11.7$	$86.9 \pm 11.4$	$93.0 \pm 11.5$	0.017
Fasting glycemia [mg/dl] [SD]	$90.2 \pm 14.2$	$86.4 \pm 10.0$	$96.7 \pm 17.7$	0.000
Glycemia 120 min post-load [mg/dl] [SD]	$130.7 \pm 45.9$	$106.5 \pm 20.63$	$172.6 \pm 47.6$	0.000
$\text{HbA}_{1c}$ (%)	$5.4 \pm 0.6$	$5.3 \pm 0.4$	$5.6 \pm 0.5$	0.005
CRP [mg/l; SD]	$2.2 \pm 3.2$	$1.3 \pm 1.7$	$3.7 \pm 4.4$	0.003

SD — standard deviation; BMI — body mass index; CRP — C-reactive protein



**Figure 2.** Mean HbA<sub>1c</sub> values in patients with glucose metabolism disorders (GMD) and in subjects with normal blood glucose. Mean HbA<sub>1c</sub> was significantly higher ( $p < 0.024$ ) in the GMD group and was 5.5%



**Figure 3.** Mean CRP level in patients with glucose metabolism disorders (GMD) and in subjects with normal blood glucose. In the GMD group, mean CRP level was 1.3 mg/L, which was significantly higher than in patients without GDM ( $p < 0.003$ )

**Table 2.** The results of gastroscopy in the examined group according to the presence or absence (healthy subjects) of glucose metabolic disorders

Pathology	Total (n, %)	Healthy subjects (n, %)	Patients with GMD (n, %)	p
<i>Helicobacter pylori</i>	23 (25.5)	8 (14)	15 (45.5)	0.001
Gastritis	8 (9)	4 (7)	4 (12)	0.412
Gastric cancer	1 (1)	0 (0)	1 (3)	0.186
Gastro-esophageal reflux	3 (3)	3 (5)	0 (0)	0.180
Hiatal hernia	5 (5.5)	3 (5)	2 (6)	0.873
Gastric polyp	1 (1)	1 (1.7)	0 (0)	0.444
Total	41 (45.5)	19 (33)	22 (67)	0.002

All patients underwent gastroscopy and abnormal results were found in 41 patients (45.5% of total study population) — in 67% in the group with GMD and 33% in the group without GDM. The most frequent pathology was *Helicobacter pylori* infection (25.5%). This infection was more prevalent in the group with GDM (45%) than in the group without GDM (14%). In addition, gastritis, gastric cancer, gastro-esophageal reflux, hiatal hernia, and gastric polyps were found, without significant differences between the subgroups (Table 2).

## Discussion

The aim of presented study was to assess the prevalence of glucose metabolism disorders (GMD) in patients with dyspepsia. Glucose metabolism disorders were diagnosed in 36.5% of patients — impaired

fasting glucose in 5.5%, impaired glucose tolerance in 22% and type 2 diabetes in 9% of patients. According to IDF from 2017, 8.8% of the world's population suffers from diabetes, of whom 87–91% have type 2 diabetes [2]. In Poland, the prevalence of diabetes is on average 3.5% [1].

The results of our study indicate that the prevalence of glucose metabolism disorders among people with dyspepsia who consider themselves healthy is surprisingly high. This means that in patients with dyspepsia, diagnostic tests for diabetes should be considered. It should be emphasized that, although patients with GMD had higher mean values of random blood glucose, this value did not exceed the normal value, which did not allow for identifying GDM patients at this stage of the study. Only in 5.5% of people with GMD, fasting

blood glucose was abnormal. It was only the OGTT result that made it possible to detect patients with GMD.

This observation confirms previous suggestions of many authors that patients should be screened for glucose metabolism disorders [3] and that the diagnosis should be based on OGTT results, not only on random blood glucose or fasting blood glucose, as their results may remain normal in patients with GMD [4].

In the examined population, pathological findings in gastroscopy, such as *Helicobacter pylori* infection, gastro-esophageal reflux, gastric cancer, gastroenteritis, hiatal hernia, were observed in 45.5% of patients. Taking into account only the group with GDM, these abnormalities were found in 66.5% of patients. However, when considering only organic lesions (excluding *Helicobacter pylori* infection), abnormal results were found only in 21%. Therefore, it should be noted that dyspepsia is mainly functional in nature and that *Helicobacter pylori* infection is highly prevalent (it was diagnosed in as many as 45.5% of patients with GMD). In the literature, the relationship between *Helicobacter pylori* infection and the occurrence of metabolic syndrome has been described [5]. In a Chinese study [6], patients infected with *Helicobacter pylori* were characterized by a higher level of fasting blood glucose and higher BMI. Awareness of this correlation is particularly important, considering a study conducted by Mokhtare et al. who observed that effective eradication of *Helicobacter pylori* infection resulted in a reduction in fasting blood glucose and HbA<sub>1c</sub>, improvement in lipid profile and reduction in waist circumference [7]. It means that thanks to the treatment of *Helicobacter pylori* infection, there is a potential chance of improving the prognosis in a large group of patients participating in our study.

According to the authors' knowledge, the prevalence of GMD among patients with dyspepsia has not been assessed previously, and the problem of prevalence of dyspeptic disorders among patients with diabetes is widely discussed in the literature [8–10]. In our study, only 4.5% of diabetic patients had abnormal results of gastroscopy (except for *Helicobacter pylori* infection). This observation is similar to the results of other studies in which dyspepsia has been found to be predominantly functional in diabetes, and long-term poor metabolic control in diabetes leads to the development of gastroparesis [8, 9, 11]. Osicpenko et al. showed that dyspepsia affects up to 71% of patients with type 2 diabetes, and in 42%, organic changes in the digestive tract were confirmed [8]. Dyspepsia was correlated with the duration of diabetes and the presence of other complications. In the study of Marizy Faria et al., the relationship between type 1 diabetes and dyspepsia was examined. Also in this study, endo-

scopic examination of the upper gastrointestinal tract revealed organic changes in 34% of patients. In addition, as in our study, the association of dyspepsia with higher levels of HbA<sub>1c</sub> was observed: in the group with GMD, HbA<sub>1c</sub> was significantly higher than in the group without GDM. The authors also link the occurrence of dyspepsia symptoms with worse glycemic control in the majority of patients [9, 10].

Another interesting relationship revealed by our study is the significant association of higher CRP and obesity with GMD occurrence. Patients with GMD had a significantly higher CRP level and a high BMI index. Similar correlations were found in a study by Christina et al. [12] who observed a significant relationship between hsCRP and the risk of developing diabetes: elevated hsCRP increased by 40–50% the risk of developing diabetes within 15 years of follow-up. Also in the Atherosclerosis Risk in Communities (ARIC) study, inflammation was strongly correlated with the development of diabetes regardless of other factors, including obesity [13]. Obesity is a recognized risk factor for the development of type 2 diabetes. In the ARIC study mentioned above, obese patients had a 6-fold higher risk of developing diabetes. However, the mechanisms responsible for this phenomenon are not fully explained [14]. The relationship between obesity and elevated inflammatory parameters is so strong that obesity is considered a pro-inflammatory factor [12, 15]. Numerous reports indicate that inflammation caused by obesity may be a link between obesity and the development of diabetes [13, 16, 17]. Hotamisligil was the first author who proposed this hypothesis, already in 1994 [18]. It is suggested that obesity leads to changes in the expression of some genes in adipocytes, which makes them produce many pro-inflammatory cytokines [15]. Inflammation causing and enhancing oxidative stress leads to dysfunction of pancreatic beta-cells [16]. Also the importance of reduced levels of adiponectin [17] — a factor that reduces inflammation and increases insulin sensitivity of tissues — in obesity is emphasized [19]. Moreover, the results of our study confirm the existence of association between glucose metabolism disorders and obesity, and an additional link intensifying these unfavorable relationships may be co-existing *Helicobacter pylori* infection, being another pro-inflammatory factor.

## Conclusions

Over 1/3 of the subjects with dyspepsia had prediabetes or diabetes; therefore, it seems that this group of patients should be screened for glucose metabolism disorders. High prevalence of GMD among patients with dyspepsia indicates potential benefits of perform-

ing OGTT in this group of patients. Gastrointestinal symptoms may be an early manifestation of glucose metabolism disorders. There is a correlation between *Helicobacter pylori* infection and the presence of glucose metabolism disorders.

### Conflict of interest

The authors declare no conflicts of interest in relation to this article.

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