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Clinical features, anxiety and depression among patients with irritable bowel syndrome with constipation and Hashimoto's thyroiditis with hypothyroidism

Objective — to determine the peculiarities of clinical characteristics, assessment of anxiety and depression prevalence in patients with irritable bowel syndrome with constipation (IBS-C) and Hashimoto's thyroiditis with hypothyroidism.

Materials and methods. 96 patients with IBS-C were included in the clinical prospective study and were divided into 2 groups: 65 (67.7 %) patients with IBS-C and Hashimoto's thyroiditis with hypothyroidism (study group) and 31 (32.3 %) patients with IBS-C (control group). Clinical examination findings were analyzed with help of questionnaires. The Hospital Anxiety and Depression Scale (HADS) was used to identify anxiety disorders and depression. Statistical analysis was performed using Stata 11 and Statistica 6 software packages.

Results. Patients with irritable bowel syndrome with constipation (IBS-C) and Hashimoto's thyroiditis with hypothyroidism were more likely to have bloating than patients with isolated irritable bowel syndrome with constipation ($p < 0.05$), who are more likely to have heartburn. No statistical difference was observed between the frequency of nausea, vomiting, pain or heaviness in stomach and loss of appetite in both groups ($p > 0.05$). Anxiety was significantly more prevalent in patients with IBS-C and Hashimoto's thyroiditis with hypothyroidism ($p = 0.002$). No statistical difference was observed between the frequency of depression in both groups ($p = 0.180$).

Conclusions. It's more likely that patients with IBS-C and Hashimoto's thyroiditis have higher frequency of bloating and higher anxiety level than patients with isolated IBS-C, in which heartburn is predominantly observed. There was no significant difference in depression level between patients with IBS-C and Hashimoto's thyroiditis and patients with isolated IBS-C.

Keywords: irritable bowel syndrome, constipation, Hashimoto's thyroiditis, hypothyroidism, bloating, nausea, vomiting, heartburn, depression, anxiety.

Irritable bowel syndrome (IBS) is one of the most common disorders in gastroenterology practice. T. Zhang et al., notes that at least 15 % of the world population suffers from IBS, and C. Canavan et al. found that approximately 30 % of those patients may visit a medical doctor [2, 16]. The scientific interest is focused on studying IBS with constipation (IBS-C) because of progressively growing need for using laxative and significant impact on the quality of life.

M. Khadka et al. concluded that there is high incidence of thyroid dysfunction in patients with IBS with constipation (IBS-C) [10]. I. Aziz and M. Simrén note the high frequency of dyspeptic symptoms in patients with IBS-C [1]. The IBS-C can severely

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affect the quality of life, mostly by influencing its physical, mental and social components. The emotional status of patients that have comorbid IBS and Hashimoto's thyroiditis is still not deeply studied. It is known that constipation can be a sign of hypothyroidism, but how these pathologies may clinically interfere each other seems not so clear.

Objective — to determine the peculiarities of clinical characteristics, assessment of anxiety and depression prevalence in patients with irritable bowel syndrome with constipation and Hashimoto's thyroiditis with hypothyroidism.

Materials and methods

This clinical prospective research included 96 patients with IBS-C divided into 2 groups: study group — 65 patients with IBS-C and Hashimoto's thyroiditis with hypothyroidism (23 (35.4 %) men, 42 (64.4 %) women, mean age 37.9 ± 13.3 years), control group — 31 patients with IBS-C (12 (38.7 %) men, 19 (61.3 %) women, mean age 40.7 ± 15.2 years). The statistical differences in age were not found between the studied groups ($p > 0.05$). All patients provided written informed consent before being enrolled into the study. The inclusion criteria were age > 18 years, IBS-C according to the Rome IV Consensus, serum TSH level of 1.0—2.5 mIU/L. The study included patients, which receive replacement therapy with L-thyroxine and achieved the drug-compensated stage of hypothyroidism confirmed by laboratory tests. The exclusion criteria were patients with recent use of antibiotics, history of taking psychotropic drugs including the supplements, history of inflammatory bowel disease, Hashimoto's thyroiditis with transient hyperthyroidism, pregnancy, history of any cancer.

We evaluated and compared the clinical symptoms between 2 studied groups such as pain or heaviness in stomach, bloating, loss of appetite, heartburn, nausea, vomiting. Evaluation of the anxiety and depression level was performed with HADS tools. The Ukrainian version of the HADS questionnaire were printed and given to each patient directly by the physician. The HADS score was interpreted as the following: 0—7 — absence of pathology; 8—10 — subclinical level of anxiety/depression; 11—21 — clinical anxiety/depression.

The diagnosis of Hashimoto's thyroiditis was established by ultrasound investigation of a thyroid gland, Thyroid-stimulating hormone (TPO) and antibodies to thyroglobulin (Anti-hTg) blood tests. Complete blood count was provided by Mispa count Plus of Agappe Diagnostics Switzerland GmbH (Switzerland); stool analysis was provided with the help of CITO TEST Fecal Occult Blood (FOB) Some patients were provided biochemical blood test including on Respons 940 of DiaSys Diagnostics System GmbH (Germany), fecal calprotectin, 12-channel ECG by 600 G of Heaco LTD (China). Abdominal ultrasound investigation was performed with Mindray Diagnostic Ultrasound System DC-80 of Shenzhen Mindray Bio-Medical Eiectronics Co (China).

Xi-square test was used to assess frequency response, and Wilcoxone and Mann-Whitney U-test — to assess mean values. All statistical analysis methods were assessed with a given error threshold level of $p < 0.05$. The statistical analysis was made with the Stata 11 and Statistica 6 programs. The Shapiro-Wilk test was used to check the normality and showed that the distribution was different from normal. Due to the presence of multiple levels of changes, the Bonferroni method was reduced to a significance level. There were 3 levels — between groups, between gender differences in the population, between gender difference in control and study groups, then the significance level was calculated, which indicates the presence of a statistically significant difference should be no less than 0.0166.

Results

The clinical characteristic of patients was assessed due to the following symptoms — pain or heaviness in stomach, bloating, loss of appetite, heartburn, nausea and vomiting.

Table 1 shows data on the frequency of gastrointestinal symptoms in both groups of patients.

The statistical analysis revealed that bloating was more prevalent in the study group than in the control group ($p = 0.000$). But heartburn observed at 51.6 % patients of control group, which is higher than in patients of study group ($p = 0.0014$). No statistical difference was observed between the frequency of nausea, vomiting, pain or heaviness in stomach and loss of appetite in both groups ($p > 0.05$). Additionally, the symptoms were compared in female and male patients of both groups. Women of study group showed more bloating ($n = 37$, 88.1 %) than the women in control group ($n = 10$, 52.6 %) ($p = 0.002$). The bloating was detected in 100 % of men of study group ($n = 23$) and 58.3 % men of control group ($n = 7$) ($p = 0.001$). The loss of appetite was different in men of study group ($n = 18$, 78.3 %) compared to the control group ($n = 4$, 33.3 %). The significant difference in prevalence of loss of appetite in both groups was not detected ($p > 0.05$).

Table 2 shows data on the frequency of anxiety and depression in both groups of patients.

Table 1. **Gastrointestinal symptoms**

Symptoms	Study group (n = 65)	Control group (n = 31)	p (χ^2-test)
Pain or heaviness in stomach	63 (96.9 %)	27 (87.1 %)	0.063
Bloating	60 (92.3 %)	17 (54.8 %)	0.000
Loss of appetite	21 (32.3 %)	9 (29.0 %)	0.746
Heartburn	17 (26.2 %)	16 (51.6 %)	0.014
Nausea	37 (56.9 %)	12 (38.7 %)	0.095
Vomiting	16 (24.6 %)	7 (22.6 %)	0.827

Table 2. **Evaluation of anxiety and depression level in patients (according to HADS)**

Characteristics	Study group (n = 65)	Control group (n = 31)	p
Anxiety, points (M ± SD)	10.45 ± 3.04	8.23 ± 3.38	0.002
0—7 (no anxiety)	10 (15.4 %)	14 (45.2 %)	0.007
8—10 (subclinical anxiety)	23 (35.4 %))	8 (25.8 %)	
11—21 (clinically significan anxiety)	32 (49.2 %)	9 (29.0 %)	
Depression, points (M ± SD)	6.35 ± 3.15	7.42 ± 3.58	0.180
0—7 (no depression)	46 (70.8 %)	18 (58.1 %)	0.118
8—10 (subclinical depression)	14 (21.5 %)	6 (19.4 %)	
11—21 (clinically significant depression)	5 (7.7 %)	7 (22.6 %)	

Men of the study group showed the highest prevalence of clinically significant anxiety (n = 14, 60.87 %), while the men of control group showed only 16.6 % prevalence (n = 2). Among women of study group the clinical anxiety was diagnosed in 42.86 % (n = 18), 16 respondents (38.09 %) showed subclinical anxiety and 9 patients (47.36 %) didn't have signs of anxiety. Depression was diagnosed in 30 respondents of women in study group (71.42 %) and 10 women (52.63 %) of control group. Among men in study group the clinically significant depression was diagnosed in only 1 patient (4.35 %), while 16 patients (69.56 %) didn't have signs of depression.

According to the results of statistical analysis, the anxiety level in patients with IBS-C and Hashimoto's thyroiditis with hypothyroidism was higher than in patients with isolated IBS-C ($p = 0.002$). The detailed analysis revealed the significant prevalence of clinically significant anxiety level in men of the study group compared to men of control group ($p < 0.05$). The statistically significant difference between women of control and study group was not detected. The difference in depression level in patients of control and study group was also not detected ($p = 0.180$).

Discussion

The current study was first to assess the relationship between Hashimoto's thyroiditis with the compensated hypothyroidism and IBS-C, established due to Rome IV criteria in Ukrainian population. B. Ohlsson et al. supposed the presence of autoimmune origins in IBS, which forced further investigating of IBS with comorbid autoimmune diseases [11]. Other studies suppose the autoimmune activity during the IBS, which can relate to the gut microbiome alterations [8, 14]. It is also confirmed that the increase level of specific antibodies is observed in patients with IBS with constipation [7]. In our study, the dyspeptic symptom such as bloating is detected in patients with IBS-C and Hashimoto's thyroiditis with hypothyroidism ($p < 0.05$). The case-control study by A. C. Ford et al. concluded that patients with functional gastrointestinal disorders have higher prevalence of autoimmune disorders [4]. A. Yesilova et al. claims that dyspeptic symptoms such as abdominal pain and discomfort are experienced by the patients with Hashimoto's thyroiditis with hypothyroidism [15]. However, in their study, which included 260 Turkish women any increase in IBS incidence in euthyroid patients

wasn't observed, as well as severity of the IBS didn't depend on the thyroid hormones level. C.S. Hsu et al. revealed that IBS was highly prevalent in patients with GERD-related dyspeptic symptoms [5]. The current study detected that prevalence of abdominal pain and discomfort didn't depend on the presence of Hashimoto's thyroiditis with hypothyroidism ($p = 0.063$). M. Khadka et al. points the high prevalence of dyspeptic symptoms in patients with IBS and thyroid dysfunction. It was described that eructation, nausea, vomiting and epigastric pain were associated with the increased level of thyroid hormones [10].

Also, our research observed higher anxiety level in patients with IBS-C and Hashimoto's thyroiditis with hypothyroidism. Z. Hu et al. pointed that patients with IBS-C show the highest level of anxiety (40.0 %) and depression (38.0 %), in comparison with other types of IBS [6]. G. Fond et al. found that high anxiety level was present in patients with IBS-C and IBS-D (diarrhea), while the increased depression level was more frequently observed in patients with IBS-D [3]. E.M. Siegmann et al. meta-analysis confirms the frequent presence of anxiety and depression disorders in patients with Hashimoto's thyroiditis [12]. J. Karmisholt and S. Andersen studied the change in the HADS score during the dynamic monitoring of patients with subclinical hypothyroidism, but there was no significant difference in mood-related symptoms measured by HADS and hypothyroid score [9]. Therefore, studying the patient-reported outcomes for knowing past medical history and complaints, defining the level of anxiety or/and depression with the help of specific measuring instruments for these patients is an actual approach, which might open new opportunities for diagnostics and treatment.

Limitations. The research was conducted in Ukraine from September 2021 till the July 2023, which was coincided with the Russian invasion to Ukraine, which points that the general anxiety level in the Ukrainian population was higher. Also in this work we didn't use the abdominal pain intensity scale, which didn't allow us to compare the intensity of pain in both groups.

Conclusions

Hypothyroidism is an important factor that may have an impact on the clinical course of IBS-C. In patients with IBS-C and Hashimoto's thyroiditis with hypothyroidism, bloating is observed significantly more often among the clinical symptoms compared to patients with IBS-C, who are more likely to have heartburn. Patients with IBS-C and Hashimoto's thyroiditis with hypothyroidism have a statistically higher frequency of anxiety compared to patients with IBS-C. Patients with IBS-C and Hashimoto's thyroiditis with hypothyroidism and patients with IBS-C do not statistically differ in the level of depression.

Conflicts of interest: none.
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acquisition of data, analysis, and interpretation of data — J.A.O.;
drafting the article, critical revision of the article — G.A.S., V.M.B., N.P.K., S.V.S., Y.A.O.

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Клінічні особливості, тривога та депресія у пацієнтів із синдромом подразненого кишечника із запорами та тиреоїдитом Хашимото із гіпотиреозом

Мета — визначити особливості клінічних виявів та оцінити поширеність тривоги й депресії в пацієнтів із синдромом подразненого кишечника із запорами (СПК-З) та тиреоїдитом Хашимото з гіпотиреозом.

Матеріали та методи. У клінічне проспективне дослідження було залучено 96 пацієнтів із СПК-З, яких розподілили на дві групи: 65 (67,7 %) пацієнтів із СПК-З та тиреоїдитом Хашимото з гіпотиреозом (дослідна група) та 31 (32,3 %) пацієнт із СПК-З (контрольна група). Для аналізу клінічних виявів використовували анкетування. Рівень тривоги та депресії оцінювали із застосуванням The Hospital Anxiety and Depression Scale (HADS). Статистичну обробку проводили за допомогою пакетів програм Stata 11 та Statistica 6.

Результати. Пацієнти із СПК-З та тиреоїдитом Хашимото з гіпотиреозом частіше мали здуття живота, ніж пацієнти контрольної групи ($p < 0,05$), тоді як останні частіше скаржилися на печію. Статистично значущої різниці за частотою нудоти, блювання, тяжкості чи болю в епігастрії та втрати апетиту між групами не виявлено ($p > 0,05$). Тривога набагато частіше траплялася в пацієнтів із СПК-З та тиреоїдитом Хашимото з гіпотиреозом ($p = 0,002$). Статистично значущої різниці за частотою депресії між групами не зафіксовано ($p = 0,180$).

Висновки. Гіпотиреоз є важливим чинником, який може впливати на клінічний перебіг СПК-З. Здуття живота значно частіше фіксували в пацієнтів із СПК-З та тиреоїдитом Хашимото з гіпотиреозом порівняно з пацієнтами лише із СПК-З, у яких частіше реєстрували печію. Частота тривоги була вищою в пацієнтів із СПК-З та тиреоїдитом Хашимото з гіпотиреозом. За рівнем депресії дослідна та контрольна групи статистично значущо не відрізнялися.

Ключові слова: синдром подразненого кишечника, запор, печія, здуття живота, нудота, блювання, біль в епігастрії, тиреоїдит Хашимото, гіпотиреоз, тривога, депресія.

ДЛЯ ЦИТУВАННЯ

Onofrijchuk JA, Solovyova GA, Bogomaz VM, Kozak NP, Skrypnychenko SV, Onofrijchuk YA. Clinical features, anxiety and depression among patients with irritable bowel syndrome with constipation and Hashimoto's thyroiditis with hypothyroidism. Modern Gastroenterology (Ukraine). 2024;1:14-18. http://doi.org/10.30978/MG-2024-1-14.