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Depressive and anxiety symptoms in patients with celiac disease – co-occurrence and mutual dependencies

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Summary

It is estimated that approximately 1% to 3% of people in the world suffer from celiac disease, which mainly affects Caucasians. The HLA-DQ2 and HLA-DQ8 haplotypes present in the majority of the European population diagnosed with celiac disease are helpful in diagnosing the disease. The main symptom is chronic inflammation of the small intestine and atrophy of the intestinal villi, but neurological and psychopathological symptoms, such as depression or severe anxiety, may also occur. Numerous studies show that a gluten-free diet alleviates the psychological symptoms associated with celiac disease. However, strict dietary requirements often constitute a challenge for patients, changing their current lifestyle and limiting its comfort. In patients with celiac disease, increased symptoms of depression and anxiety are observed, and the duration of the disease affects the severity of the above symptoms. Currently, therapeutic benefits are attributed especially to a gluten-free diet, but recent scientific reports indicate a comparable clinical effect in patients using probiotics. The course of the disease is also influenced by the emotional support of the patient's family, causing a milder course of the disease. Caregivers of patients should pay special attention to the symptoms of anxiety and depression in their patients, because they are often unnoticed, which leads to an unfavourable course of the disease.

Key words: celiac disease, depression, gluten intolerance

Introduction

An autoimmune disease is a disorder in which the body's immune system mistakenly recognises its own cells, including entire groups of them, treating them as foreign, which results in the activation of an immune response. An example of such

a condition is celiac disease (CD), which belongs to a group of chronic immunological diseases, provoked by the consumption of gluten by people with genetic predisposition. This results in a T-cell mediated response and production of autoantibodies that cause inflammation of the small intestine and atrophy of intestinal villi [1]. The term gluten allergy, next to celiac disease, is the second most common type of gluten intolerance and refers to a rapid autoimmune reaction via immunoglobulin E that occurs during contact with wheat. On the other hand, non-immunological gluten sensitivity is a term referring to the body's reaction that does not have an immunological basis. The symptoms of this hypersensitivity are similar to those of celiac disease and gluten allergy, but do not meet the diagnostic criteria for these conditions [2, 3].

Celiac disease has many non-specific symptoms involving several organ systems. The main symptoms include: enteropathy, gastrointestinal symptoms and fatigue [4, 5]. People with celiac disease often experience mental disorders, mainly related to anxiety and depressive symptoms [6]. According to the guidelines of the European Society of Paediatric Gastroenterology, Hepatology and Nutrition, the initial test for the diagnosis of celiac disease should be the determination of deaminated gliadin peptide antibodies (DGP-IgG/IgA), it is also recommended to determine the concentration of total IgA and antibodies against transglutaminase class 2 IgA (TGA-IgA). If TGA-IgA is ten times higher than the norm and there is a positive family history – celiac disease can be diagnosed without biopsy. Biopsy is required if TGA-IgA is exceeded less than ten times the norm. Four biopsies should be taken from the distal part of the duodenum and at least one from the duodenal bulb [7].

The basis for minimising the symptoms of celiac disease is the introduction of a gluten-free diet, which is the basis of the treatment of this disease. Although it is not recommended for healthy people, it is increasingly used in practice. A properly maintained gluten-free diet can positively affect the quality of life and health of patients with celiac disease [8]. Taking preventive measures to quickly identify symptoms of depression and anxiety in people with CD helps prevent the persistence of symptoms and counteracts the negative effects experienced by patients.

Epidemiology of celiac disease

According to available data, between 1% and 3% of people worldwide struggle with celiac disease. This phenomenon can be observed in people of Caucasian origin, as the disease is rare among Asians, including the population living in China or Japan [9]. Over the last 10-25 years, there has been a significant increase in the number of celiac disease diagnoses [10]. This development is most likely due to a specific set of genes present in patients, predisposing them to this disease. Genetic studies show a particularly clear presence of the HLA-DQ2 and HLA-DQ8 haplotypes. A pan-European study showed that only 0.4% of celiac patients were not carriers of DQ8 and DQ2 [11].

Gender also plays a significant role in epidemiology, as women are more likely than men to develop celiac disease. It is estimated that around 1% of Europeans struggle with the consequences of the disease [12]. Celiac disease is increasingly being diagnosed in children, but most cases are diagnosed in people between 20 and 30

years of age [13]. In addition, children with celiac disease autoimmunity, especially when they have a complete set of HLA-DQ2 and HLA-DQ8 alleles, may experience anxiety problems and oppositional-defiant behavior [14].

Purpose and method

The aim of the following work was to organise the current knowledge on the co-occurrence of celiac disease and emotional disorders, and to attempt to determine the mutual dependencies between these diseases. Review of works was performed using the following platforms: PubMed, Google Scholar and National I. When searching for publications, the following phrases were used: 'depression in celiac disease', 'depression in caregivers of celiac patients', 'differences in the perception of depression in patients with celiac disease', 'the role of anxiety in celiac disease', 'stress in celiac disease', 'the effect of diet on celiac disease symptoms', 'gluten-free diet in celiac disease effects on depression', 'neurosis in celiac disease', 'anxiety in celiac disease'. The work is of an illustrative nature, prepared according to PRISMA principles. The material intended for analysis was collected from February 24 to April 15, 2024. The analysis included works published in Polish and English. During the initial selection of scientific papers, the substantive assessment was made on the basis of the abstract. Items that did not directly concern the described issue were rejected, as well as works published more than fifteen years ago. The excluded items also included works without free online access. The analysis was made on the basis of publications from the last 15 years to use the latest data.

The literature review on the impact of celiac disease on mental health included 53 articles. The analysed studies included a variety of methodological approaches, including meta-analyses and systematic reviews (16), cohort studies (7), cross-sectional studies (14), randomised controlled trials (1), case reports (2), methodological/other papers (6). The aim of these studies was to investigate the association of celiac disease with emotional disorders such as depression, anxiety and stress, as well as the impact of a gluten-free diet on the mental health of patients.

Only those studies that reported the association of celiac disease with emotional problems or analysed the impact of a gluten-free diet on mental health were finally included in the review. These studies included both adults and children with celiac disease, including their caregivers. An important inclusion criterion was the presence of a control group. On the other hand, studies that did not show an association with celiac disease or emotional disorders, did not have a control group, only reported NCGS (Non-Celiac Gluten Sensitivity) without considering celiac disease, or had unclear methodology and ambiguous results that could complicate interpretation, were excluded from the analysis. Figure 1 below presents the procedure for selecting articles for analysis.

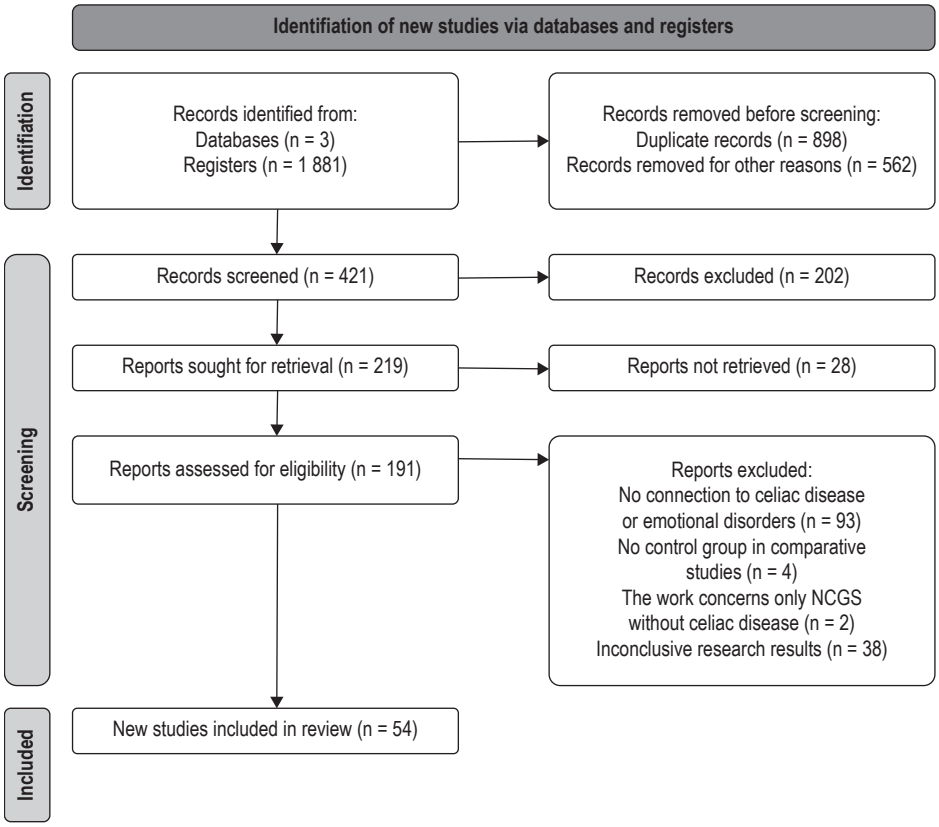

Figure 1. **The method of selecting scientific publications that were included in the article according to the PRISMA scheme [15]**

Due to the multifactorial impact of celiac disease on the mental state, the problem of co-occurrence of depressive and anxiety symptoms with celiac disease symptomatology was considered based on selected aspects of the functioning and treatment of these patients. For this purpose, the influence of the gut-brain axis and the influence of a gluten-free diet on the intensification of depressive symptoms were described. During the review of scientific papers, it was noted that important issues raised in the context of patients is the induction of depression in caregivers of patients with celiac disease. The authors also assessed the importance of support for patients with celiac disease and its influence on reducing depressive symptoms in these patients. The paper also draws attention to differences in the perception of psychiatric disorders in patients with celiac disease by the patients themselves and their caregivers. The following paper aimed to broadly analyse the relationship between celiac disease and depressive and anxiety symptoms, including the impact of this disease and its treatment on the occurrence of depressive disorders.

The role of the gut-brain axis in inducing psychopathological symptoms in patients with celiac disease

Symptoms of depression and anxiety often accompany patients suffering from celiac disease. However, the pathophysiology responsible for psychological disorders coexisting with celiac disease has not been fully understood [16]. Studies on HLA molecules present in celiac disease provide information on the progression of the impaired immune response caused by exposure to gluten, which consequently leads to the development of celiac disease. Celiac disease belongs to a group of autoimmune dysfunctions that are caused by the consumption of gluten, which acts as an irritant to the immune system in people with a genetic predisposition [17]. The main symptom characteristic of this disease is chronic inflammation of the small intestine, which results in atrophy of intestinal villi. Symptoms of the disease are not limited to the digestive system, they can also affect the nervous system and coexist with mental disorders. Current gastrointestinal disorders (GID) often accompany symptoms of depression and anxiety, and experiencing long-term pain coexisting with inflammation affects certain areas of the brain, including the anterior cingulate cortex (ACC). This place is particularly sensitive to signals sent by inflamed nerves, which can lead to a worsening of mood and impairment of cognitive functions [18].

Persistent inflammation of peripheral nerves in patients with celiac disease may contribute to an increased sense of threat, sensitivity to pain in the ACC, which in consequence leads to an unfavourable, long-term structural reconstruction of this part of the brain along with an increase in the intensity of threat signals felt by the patient. Overinterpretation of received stimuli by a sick person, even in the absence of significant indications of a possible threat, causes anxiety. The anterior cingulate cortex of the brain operates on patterns, predicting affective outcomes, in this case, experienced pain, based on complex contextual information [19]. Processing information in this way can affect the autonomic nervous system, exacerbating immune dysfunction and leading to development of gastrointestinal dysfunction. Studies conducted on animal models provide information on analogous changes in the brain and behaviour that are observed in the human population. Despite the lack of highly developed cognitive abilities, unlike humans, rodents present reliable behaviours, both adaptive and maladaptive, similar to those observed in patients suffering from ACC inflammation [20].

Studies conducted so far on laboratory rats show that inflammation and intestinal dysfunctions influence changes in behaviour and neuronal activity [21]. They manifest themselves in problems with coping with stress, experiencing constant anxiety with episodes of depression. As Campagna et al. [22] report in their review, cognitive impairment and other psychopathological symptoms are more common in people who do not undergo treatment for celiac disease compared to patients who use treatment recommended for the course of the autoimmune disease [22].

Does a gluten-free diet used by patients with celiac disease affect the intensity of symptoms of mental disorders?

Within the last few years, gluten has been increasingly excluded from the diet, which has contributed to the use of gluten-free diets on a global scale. An example of a country where the gluten-free diet has dominated the market is the United States, where in 2013 30% of adult residents declared that they would limit or completely eliminate gluten from their diet. This trend has led to an increase in the frequency of self-diagnoses among people interested in this type of diet and numerous diagnoses of the disease by people who do not have the appropriate professional qualifications and knowledge. This has led to an increase in the group of people with celiac disease by people who do not suffer from gluten intolerance [23]. An important aspect of using a gluten-free diet is the need to balance it. Studies have shown that people on a gluten-free diet may experience deficiencies in B vitamins, vitamin D, iron, magnesium, potassium, and calcium, which are important for the functioning of the nervous system and mental health [24].

The potential relationship between social anxiety and celiac disease and the effect of gluten-free diet (GFD) used in treatment was analysed in a group of adults. The study analysed the intensity of anxiety in patients, feelings related to social anxiety, and nutritional attitudes and quality of life (QOL). For this purpose, a questionnaire designed for patients was used, containing three surveys: *Development and Validation of a New Celiac Disease Quality of Life* (CD-QOL), *Social Anxiety Questionnaire for Adults* (SAQ) and *Celiac Disease Eating Attitudes and Behaviours* (CD-FAB). The results showed moderate quality of life in patients with celiac disease, with a concomitant high level of social anxiety, where 9% of the study group of 538 people exceeded the clinical threshold of social phobia. Patients using GFD for less than one year showed higher levels of anxiety and lower QOL scores. Individuals who were not in a partnership and younger were characterised by low QOL values and more severe social anxiety. The conclusions of the study show how important the problem of social anxiety is for celiac patients. Failure to follow a gluten-free diet with an accompanying sense of anxiety, may result in symptoms of depression in the later period [25].

In a study conducted by Simsek et al. [26], the effect of a gluten-free diet on the exacerbation of depressive symptoms and quality of life of 25 children with celiac disease and 25 healthy study participants was analysed. The *Depression Scale for Children* was used to assess the level of depression. The difference in the patients and control group participants in terms of the prevalence of depressive symptoms was not significant. Patients who approached the recommendations correctly and followed the GFD guidelines experienced a significant decrease in depressive symptoms compared to those who did not follow the diet. Conclusions drawn from the observations assume that following a gluten-free diet can have a positive effect on reducing the level of depression in children with celiac disease [26].

In another study on the influence of diet on the course of depressive disorders in patients with celiac disease, it was observed that the use of the Mediterranean diet (MD) is associated with an improvement in mental health among surveyed people [27].

Following this type of diet meant excluding gluten from daily meals. Women showed more severe symptoms of depression and anxiety compared to men. Most people participating in the study had a low adherence to the MD diet, which correlated with an increase in the intensity of psychopathological symptoms, especially in women [28].

Prevention of deterioration of the mental state of patients with CD involves limiting the availability of gluten in the diet. The use of a gluten-free diet by study participants with celiac disease and depression significantly improved depression parameters (SMD – 0.37). No significant differences were observed between the patient group and the control group. People with non-celiac gluten sensitivity showed an increase in the frequency of depressive symptoms as a result of gluten challenge compared to placebo (SMD 0.21) [29].

Rigorous and proper use of a gluten-free diet is associated with many difficulties and sacrifices on the part of patients with CD. Such action has a significant impact on their daily lives and those of their loved ones, which may be associated with experiencing negative emotions. Another study focused on the consequences of using a GFD in relation to the lifestyle and emotional functioning of patients with celiac disease [30]. Full adherence to a gluten-free diet was declared by 56% of the study participants from a group of 222 patients, while the group of healthy people included 36 people consuming gluten. The impact of GFD on social functioning was small, but patients eating meals at home showed a sense of isolation due to the limited possibility of eating them in a restaurant. Healthy participants of the study used the services of a doctor to a lesser extent, experienced lower levels of negative emotions, including depression, and showed joy associated with eating, which was not observed in patients with celiac disease [30].

Improved mental health after eliminating gluten from the diet in people who are allergic to this protein can be observed in the so-called gluten psychosis. The disease entity, the so-called: non-celiac gluten sensitivity (NCGS), is usually confirmed by eliminating gluten from the diet [31]. If the health condition of the person we suspect the syndrome improves with gluten-free food, then after excluding celiac disease and allergies, we can diagnose NCGS. The main non-gastric symptoms present in non-celiac gluten sensitivity include nervous system dysfunctions and episodes of depression. One of the hypotheses explaining the relationship between gluten sensitivity and psychopathological symptoms assumes the possibility of protein penetration through the intestinal membrane, penetration into the circulation, and then crossing the blood-brain barrier. There, gluten may act on neurotransmission through the endogenous opioid system [32]. However, this relationship has not been confirmed, and the diagnosis of NCGS is still hampered by the lack of a specific biomarker that would allow for an unambiguous diagnosis [33]. An example of the far-reaching consequences of undiagnosed celiac disease is the case of a 47-year-old patient. The patient was hospitalised several times due to psychomotor hyperactivity and suicide attempts, additionally did not respond to pharmacological and electroconvulsive therapy. Detailed diagnostics revealed the presence of CD in the patient, and the use of a gluten-free diet alleviated the neurological and psychiatric symptoms after only two months [34].

The influence of probiotic use in celiac disease patients on the course of the underlying disease

In patients with celiac disease, therapeutic benefits are mainly due to a gluten-free diet, but recent studies report a beneficial effect of probiotics on the course of celiac disease. Available literature shows that before the first symptoms of the disease appear, there is an increase in the number of bacteria from the *Bacteroides spp*. family and a decrease in the level of *Bifidobacterium spp*. [35]. Currently, international studies are underway on the impact of microbiota composition disorders on the development of celiac disease, which are being conducted by *Celiac Disease Genetic, Environmental, Microbiome, and Metabolomic Analysis*. The study includes newborns with a family history of celiac disease [36].

If a gluten-free diet is not completely effective, probiotics are used as an adjuvant, as they cause gluten hydrolysis, reducing the immunogenic effect of gluten [37]. In a study involving rodents, a positive effect of *Lactobacillus casei* on the condition and regeneration of damaged intestinal villi resulting from previous gliadin administration was observed. Mice were sensitised to gliadin, which resulted in damage to intestinal villi, impaired expression of TNF-alpha and a decrease in the level of gliadin-specific IL-2. Taking the probiotic resulted in the reconstruction of intestinal villi, a delay in the loss of body weight of rodents was observed, as well as the levelling of TNF-alpha levels, while the level of IL-2 did not change [38]. Strains from the *Lactobacillus* family have the ability to hydrolyse gliadin, which reduces the immunising effect and reduces the degree of damage to intestinal villi [39]. In addition, another study on gluten-sensitive mice showed increased production of COX-2, IL-15 and pro-inflammatory cytokines. Increased levels of antibodies against transglutaminase 2 were also observed, as well as the presence of damaged intestinal villi. After administration of a probiotic with the *Saccharomyces boulardii KK1* strain, reconstruction of the intestinal structure and a decrease in cytokine production were observed [40]. In 2019, a study was conducted on the effect of using a probiotic for 6 months containing *Lactobacillus plantarum HEAL9* and *L. paracasei 8700:2* in children with diagnosed celiac disease. It was noted that the progression of the effects of celiac disease was inhibited despite the consumption of gluten. The level of antibodies against tissue transglutaminase decreased significantly, which indicates a modulation of the immune response in children with celiac disease who do not follow a gluten-free diet [41]. The above studies indicate that the effects of celiac disease can be alleviated not only by following a gluten-free diet, but also by using probiotics.

Co-occurrence of celiac disease, depressive and anxiety symptoms

Celiac disease significantly worsens the mental well-being of patients and often leads to social isolation. The co-occurrence of emotional disorders worsens the prognosis of the underlying disease. Therefore, prevention aimed at early detection of depressive and anxiety symptoms plays a very important role in the care of patients with celiac disease.

A population-based study in Sweden, which involved 19,186 sick children, examined the impact of celiac disease on the development of psychiatric disorders. The frequency of depression diagnoses among celiac disease patients was 2.4% higher compared to healthy individuals, while the probability of developing psychiatric disorders was 19% higher regardless of the patient's age, compared to the healthy population. The highest incidence of depression was observed in the first year after diagnosis. The most common psychiatric problems included mood disorders, anxiety disorders, eating disorders, attention deficit hyperactivity disorder, and autistic symptoms. Attention was also drawn to an increased risk of psychiatric disorders in the later stages of the disease, which often persisted into the adulthood of patients [42].

The study by Tittel et al. [43] included selected centres in Germany, Austria, Luxembourg, and Switzerland, which included four groups of patients: (1) patients with type 1 diabetes only, (2) patients with type 1 diabetes and celiac disease, (3) patients with type 1 diabetes and depressive symptoms, and (4) patients with type 1 diabetes, depressive symptoms and celiac disease. A total of 79,067 patients participated in this project. On this basis, the risk ratio of depressive symptoms in patients with celiac disease was determined to be 1.25 and higher for women. In the group of patients with type 1 diabetes, celiac disease and depressive symptoms, autistic behaviour, attention deficit hyperactivity disorder, anxiety symptoms, eating disorders, and schizophrenia were observed more frequently compared to patients with diabetes only.

Another study involved 6,329 patients with celiac disease. It was noted that the incidence of neuropsychiatric disease in these patients increased with time from diagnosis and was 3.9% after the first year, 14.9% after five years, 24.8% after ten years and 35.9% after fifteen years, compared to the control group, in which these values were 1.8%, 9.3%, 18.3%, and 27%, respectively. Among neuropsychiatric disorders in patients with celiac disease, depressive and anxiety-related disorders, eating disorders, migraine headache episodes and epilepsy were observed particularly often [44].

In the next study, the prevalence and severity of anxiety and depressive symptoms in patients with celiac disease were assessed using the GAD-7 (*Generalised Anxiety Disorder-7*) and PHQ-9 (*Patient Health Questionnaire-9*) scales. The most frequently reported symptom was anxiety, which occurred in 85% of patients, half of whom had only mild anxiety disorders, while depressive symptoms were observed in 82.7% of patients, including 25.6% with mild depressive symptoms. Such frequent depressive and anxiety disorders drew the authors' attention to the need to diagnose mental disorders in this group of patients [45]. Belpınar et al. [46] observed anxiety symptoms in about 44% of children with celiac disease, and the occurrence of depressive symptoms was noted in 23% of them. A negative impact of anxiety on the quality of life of patients was also noted. Similar relationships were described by Carta et al. [47] much earlier, but they focused specifically on the co-occurrence of bipolar disorder with celiac disease. Among the studied people, 30% showed severe depressive symptoms, 18.3% experienced panic attacks and 4.3% experienced bipolar disorder. In the control group, the prevalence of these disorders was 8.3%, 5.4% and 0.4%, respectively. In addition, attention was drawn to the need for screening for celiac disease in people with bipolar disorder and a positive family history of celiac disease.

In a study conducted by the Polish Celiac Society [48], in which 2,500 patients participated, the impact of celiac disease on quality of life was examined using the EQ-5D (*Euro Quality of Life Questionnaire*). Chronic fatigue was observed in 63% of patients, and anaemia affected 58% of patients, while 43% of the study participants showed anxiety and depressive symptoms, and the introduction of a gluten-free diet reduced the intensity of these symptoms. The results were compared with the British population, in which depression and anxiety were less severe after diagnosis, compared with the Polish population, in which depressive symptoms accompanied by anxiety remained at a higher level both before and after diagnosis of celiac disease, which may be related to better care for patients with this condition in the UK [48].

In the analysis of the frequency of use of psychopharmaceuticals in people with celiac disease, compared to the frequency of use of these drugs in people with abdominal pain or reflux, no significant differences were observed. In turn, the frequency of use of antidepressants was higher in people with celiac disease and amounted to 16.4%, compared to people with the above-mentioned digestive disorders (13.4%). No significant relationship was observed between the time from the moment of appearance of symptoms to detection of the disease and its stage of advancement, and the time of use of antidepressants [49].

The role of caregivers in early detection of emotional disorders and family support as an important element of care for a young patient with celiac disease

The perception of emotional problems by caregivers in their charges can be very difficult and, as the studies cited below show, it is often insufficient. The aspect of emotional functioning of sick children can often be overlooked and underestimated, although it is common knowledge that early detection of disorders in this area improves the quality of life of young patients.

In a paediatric clinic, Germone et al. [50] conducted a study of celiac patients aged 8–17, in which the level of depression and anxiety was assessed using the RCADS (*Revised Children's Anxiety and Depression Scale*). The study involved 152 patients and 175 caregivers, who assessed the occurrence of depressive and anxiety symptoms in their charges. Among the examined children, these symptoms were confirmed by 39% of patients. Children with comorbidities such as atopy and endocrine disorders showed lower symptoms of anxiety and depression compared to patients without comorbidities. In turn, anxiety disorders observed by caregivers were reported in 6.9% of patients, and depressive disorders in 14.3%. Such a significant difference between the observations of adults and their children draws attention to the need to conduct an interview on depressive symptoms and anxiety not only on the basis of the caregiver's observations. It is worth noting that in the above study, less severe anxiety and depressive symptoms were observed in children with diseases coexisting with celiac disease, such as atopy and endocrine disorders, compared to patients without coexisting diseases [50], which, in the opinion of the authors of this study, requires further research. In slightly older adolescents, depressive symptoms were observed twice as often in patients with celiac disease compared to healthy individuals. The incidence of depression in

patients with celiac disease was comparable to the incidence of depression found in people treated psychiatrically. Young patients reported depressive symptoms 44% more often than their caregivers noticed. The authors of the study paid special attention to the need for screening tests for emotional disorders in this group of patients, because early detection affects the prognosis of the underlying disease [51].

Data from a systematic review [16] indicate that patients with celiac disease are at increased risk of developing autism spectrum disorders (ASD), ADHD, depressive symptoms, anxiety, and eating disorders. The correlation between ASD and ADHD in people with celiac disease is very high. For this purpose, patients with the above-mentioned psychiatric disorders, who do not have celiac disease, are recommended to follow a gluten-free diet to reduce behavioural disorders. In patients with celiac disease, depressive and anxiety symptoms are most often observed, the intensity of which significantly decreases when the person receives support from others. Emotional and social support plays a key role in reducing these symptoms, improving the patient's well-being and quality of life [16]. Another work [52] also highlights the frequent experience of anxiety and depression by patients with celiac disease. The study noted that anxiety symptoms concern 62.7% of patients, of whom 98.1% reported a lack of control over the disease, while depression occurs in 34.9% of the respondents. Half of the patients reported a lack of family support during the course of the disease, which significantly affects the deterioration of mental health. In turn, the remaining part of the respondents receiving support from their loved ones manifest only a mild course of depression [52].

In the available literature, one can also find studies on the health status of caregivers of celiac disease patients, in whom the prevalence of depressive symptoms was found to be higher than in the general population [53]. It has also been noted that depressive and anxiety symptoms are much more common in mothers whose children do not follow a gluten-free diet, compared to mothers whose children follow the recommended diet [54].

Recapitulation

The presented data show that 1 to 3% of people worldwide suffer from celiac disease, especially Caucasians. Genetic studies indicate an important set of HLA-DQ2 and HLA-DQ8 haplotypes associated with the disease, which should be considered during diagnosis. The main symptom of CD is chronic inflammation of the small intestine, leading to atrophy of intestinal villi, but neurological symptoms and deterioration of the mental state may also occur, manifested by depression and increased anxiety. Studies confirm the beneficial effect of a gluten-free diet on alleviating psychopathological symptoms coexisting with celiac disease and the so-called gluten psychosis. The use of probiotics also promotes not only the regeneration of intestinal villi but also improves the emotional functioning of patients. Selected strains of bacteria affect the breakdown of gluten and gliadin, reducing the effect of these substances on immunogenicity in the intestine, and also stimulate the regeneration of intestinal villi, improving the patient's health.

The studies presented above report an increased prevalence and greater intensity of depressive and anxiety symptoms in patients with celiac disease. Moreover, it seems that a longer duration of the disease promotes the intensification of these symptoms. However, the interrelationships between the typical symptomatology of celiac disease and the symptoms of emotional disorders are not entirely clear and require further research. It is also worth emphasising that psychopathological symptoms in young adults are not noticed by their caregivers, which affects the course of the underlying disease and the quality of life of patients.

Authors' statement: all the authors contributed equally to the work

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