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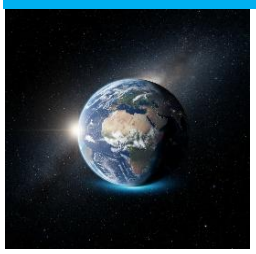

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Depression and Anxiety as Aspects of Mental Health in Celiac Disease: A Systematic Review and Meta-Analytical Synthesis

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Abstract

Background:

Celiac disease (CD) is a chronic immune-mediated disorder with significant extraintestinal manifestations, including neuropsychiatric symptoms. Depression and anxiety are among the most frequently reported and may substantially affect quality of life.

Aim:

This review aimed to evaluate the prevalence of depressive and anxiety symptoms in adults and children with CD and to assess the influence of adherence to a GFD on psychiatric outcomes.

Material and Methods:

A structured narrative review with meta-analytical synthesis was conducted using studies identified through PubMed/MEDLINE, Scopus, and Web of Science. Observational studies, clinical cohorts, and existing meta-analyses were included. Findings were integrated narratively, considering age, disease status, and dietary adherence.

Results:

Depressive symptoms were consistently more prevalent in individuals with CD, particularly in untreated or newly diagnosed patients. Partial improvement was observed following initiation of a gluten-free diet although symptoms often persisted. Findings regarding anxiety were heterogeneous. Psychiatric outcomes were influenced by disease activity, age, nutritional status, and psychosocial factors.

Conclusions:

Depression and anxiety are clinically relevant but often underrecognized components of CD. A GFD may alleviate psychological distress but does not fully eliminate psychiatric morbidity, supporting the need for routine mental health screening and multidisciplinary care.

Key words:

celiac disease; depression; anxiety; psychiatric symptoms; gluten-free diet; meta-analysis

Contents

1. Introduction

Celiac disease (CD) is a chronic, immune-mediated disorder precipitated by the ingestion of gluten-containing cereals-primarily wheat, rye, and barley-in genetically predisposed individuals. It affects approximately 1% of the global population and is characterized by small intestinal inflammation, villous atrophy, and varying degrees of malabsorption. Historically regarded as a gastrointestinal condition of childhood, CD is now recognized as a lifelong, multisystem disease that can present at any age and with a wide spectrum of intestinal and extraintestinal manifestations. Advances in serological screening and heightened clinical awareness have contributed to increased detection rates; nevertheless, a substantial proportion of cases remain undiagnosed or are identified only after prolonged disease duration.

Beyond classical gastrointestinal symptoms, CD is increasingly associated with extraintestinal complications involving the endocrine, dermatological, skeletal, and nervous systems. Among these, neuropsychiatric manifestations have gained particular attention due to their prevalence, clinical relevance, and impact on quality of life. Depression and anxiety are the most frequently reported psychiatric symptoms in individuals with CD, although other affective, cognitive, and behavioral disturbances-including bipolar spectrum disorders, panic disorder, sleep disturbances, and impaired stress regulation-have also been described. Importantly, psychiatric symptoms may precede the diagnosis of CD, coexist with active intestinal disease, or persist despite long-term adherence to a gluten-free diet (GFD), complicating both diagnosis and management.

The relationship between celiac disease and psychiatric morbidity is complex and remains incompletely understood. Several biological mechanisms have been proposed to explain this association. Chronic intestinal inflammation and malabsorption may lead to deficiencies in micronutrients and amino acids essential for neurotransmitter synthesis, such as tryptophan, folate, vitamin B12, iron, and long-chain polyunsaturated fatty acids. Immune-mediated pathways, including cytokine-driven neuroinflammation and autoimmune comorbidities (e.g., autoimmune thyroid disease), may further contribute to mood dysregulation. In parallel, alterations in the gut-brain axis, intestinal permeability, and microbiota composition have been increasingly implicated as potential mediators linking intestinal pathology with central nervous system function.

In addition to biological factors, psychosocial mechanisms play a substantial role in shaping mental health outcomes in CD. The burden of living with a chronic disease, diagnostic delays, and the necessity of lifelong adherence to a restrictive gluten-free diet may lead to social

isolation, reduced participation in daily activities, heightened health-related anxiety, and diminished overall well-being. The GFD itself, while being the cornerstone of CD treatment, can impose significant practical, financial, and emotional challenges. Consequently, the diet may act as both a therapeutic intervention and a psychosocial stressor, with heterogeneous effects on psychological health across different patient populations.

Despite a growing body of literature addressing psychiatric symptoms in CD, findings remain inconsistent. Clinical studies frequently report elevated rates of depression and anxiety, whereas some large population-based surveys suggest comparable or even lower prevalence rates relative to the general population. Pediatric and adult cohorts also appear to differ with respect to symptom profiles, disease perception, and response to dietary treatment. Furthermore, existing studies vary widely in design, diagnostic criteria, psychiatric assessment tools, and consideration of confounding variables, limiting the generalizability of individual findings.

Several systematic reviews and meta-analyses have attempted to synthesize available evidence, generally supporting an increased burden of depressive symptoms in celiac disease, while conclusions regarding anxiety remain less consistent. However, rapid growth in the literature over the past decade—particularly studies incorporating standardized psychiatric scales, pediatric populations, and adherence-related outcomes-warrants an updated and integrative evaluation. A comprehensive synthesis that simultaneously addresses age-specific differences, disease status, dietary adherence, and underlying mechanisms is needed to better inform clinical practice.

Therefore, the purpose of this article is to provide an in-depth, doctoral-level review and meta-analytical synthesis of psychiatric symptoms in celiac disease, with a primary focus on depression and anxiety. By integrating findings from observational studies, clinical cohorts, and existing meta-analyses, this review aims to clarify the magnitude and nature of psychiatric morbidity in CD, examine the role of the gluten-free diet, and discuss potential biological and psychosocial mechanisms. Improved understanding of these relationships is essential for developing multidisciplinary management strategies and optimizing both physical and mental health outcomes in individuals with celiac disease.

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2. Research materials and methods

This study was designed as a structured narrative review with a meta-analytical synthesis of previously published data. The methodological approach combined elements of a systematic review with a comparative analysis of results derived from existing meta-analyses and large observational studies. This design was chosen due to the heterogeneity of study populations, psychiatric assessment tools, and outcome measures across the literature addressing psychiatric symptoms in celiac disease.

A comprehensive literature search was conducted to identify peer-reviewed articles examining psychiatric symptoms in individuals with celiac disease. Electronic databases including PubMed, MEDLINE, Scopus, and Web of Science were searched from database inception to the most recent publications available at the time of manuscript preparation. The search strategy employed combinations of Medical Subject Headings (MeSH) and free-text terms, including but not limited to: *celiac disease*, *coeliac disease*, *depression*, *anxiety*, *psychiatric symptoms*, *mental health*, *gluten-free diet*, *psychological morbidity* and *quality of life*.

Reference lists of relevant reviews and meta-analyses were manually screened to identify additional eligible studies not captured in the primary database search. Only articles published in English were considered.

Rather than conducting a de novo statistical meta-analysis, this review integrated quantitative findings from previously published meta-analyses and large-scale pooled analyses. Effect sizes, odds ratios, confidence intervals, and heterogeneity indices reported in these studies were compared and synthesized narratively. Particular attention was paid to differences between adult and pediatric populations, untreated versus treated celiac disease, and comparisons with both healthy controls and individuals with other chronic medical conditions.
As this study was based exclusively on previously published data, no ethical approval or informed consent was required. The review was conducted in accordance with accepted standards for academic integrity and responsible research synthesis.

3. Research results

3.1. Study Selection and Characteristics

The literature search and screening process yielded a substantial body of evidence addressing psychiatric symptoms in celiac disease, including cross-sectional studies, case–control studies, cohort analyses, randomized and non-randomized interventional studies, as well as systematic reviews and meta-analyses. The included studies encompassed diverse geographic regions, primarily Europe, North America, the Middle East, and South America, and represented both adult and pediatric populations.

Sample sizes varied markedly, ranging from small clinical cohorts to large population-based surveys including several thousand participants. Psychiatric outcomes were assessed using a wide array of validated instruments, such as the Hospital Anxiety and Depression Scale (HADS), Beck Depression Inventory (BDI), State–Trait Anxiety Inventory (STAI), Patient Health Questionnaire (PHQ-9), Children's Depression Inventory (CDI), and structured diagnostic interviews based on DSM or ICD criteria. This methodological heterogeneity was a major determinant of variability in reported prevalence rates and effect sizes.

3.2. Prevalence of Depressive Symptoms

Across the majority of clinical and observational studies, depressive symptoms were more prevalent in individuals with celiac disease than in healthy control populations. Reported prevalence rates of depression in adults with CD ranged broadly, from approximately 6% to over 50%, depending on disease status, assessment method, and study design. Meta-analytical data consistently demonstrated a significantly increased risk of depressive symptoms in CD, with pooled effect sizes indicating a moderate to large association when compared with the general population.
Several studies reported that depressive disorders were particularly common in patients with untreated or newly diagnosed CD, suggesting a relationship between active intestinal disease and mood disturbance. Importantly, some large population-based surveys failed to demonstrate significantly higher rates of diagnosed depression in individuals with CD, highlighting a discrepancy between clinically recruited samples and community-based cohorts.
In pediatric and adolescent populations, elevated rates of depressive symptoms were also observed, often predating the diagnosis of celiac disease. In these cohorts, lifetime prevalence of major depressive disorder and subclinical depressive symptoms was consistently higher than

in age-matched controls, although current depressive symptomatology tended to decrease following dietary treatment.

3.3. Prevalence of Anxiety Symptoms

Findings related to anxiety were less consistent than those for depression. Many clinical studies reported increased levels of anxiety symptoms in both adult and pediatric patients with celiac disease, particularly in females and in individuals with poor disease control or persistent symptoms. Anxiety prevalence rates ranged from approximately 15% to over 60% in selected clinical samples.

However, meta-analytical evidence suggested that while anxiety symptoms may be elevated in some CD populations, overall differences between adults with celiac disease and healthy controls were not consistently significant across all studies. When comparisons were made with individuals suffering from other chronic medical conditions, anxiety levels in CD patients were often similar, supporting the hypothesis that anxiety may reflect a nonspecific response to chronic illness rather than a CD-specific phenomenon.

3.4. Impact of Gluten-Free Diet on Psychiatric Outcomes

The influence of a gluten-free diet on psychiatric symptoms emerged as a key theme across studies. Many investigations reported partial improvement in depressive and anxiety symptoms following initiation of a GFD, particularly within the first year of treatment. Improvements were more pronounced in patients with good dietary adherence and in those with severe symptoms at baseline.

Nevertheless, a considerable proportion of patients continued to experience clinically relevant psychiatric symptoms despite long-term adherence to a gluten-free diet. Some studies reported persistent depression and anxiety even after several years of treatment, indicating that dietary intervention alone may be insufficient to fully reverse psychological morbidity. In certain cohorts, strict dietary adherence was paradoxically associated with increased anxiety, likely reflecting heightened vigilance, fear of gluten exposure, and social constraints imposed by the diet.

3.5. Adult versus Pediatric Populations

Age-related differences were evident across the reviewed literature. In children and adolescents, psychiatric symptoms-particularly depressive and behavioral disturbances-were frequently observed before diagnosis and tended to improve following dietary treatment. In contrast, adults more often exhibited persistent or recurrent psychiatric symptoms, even in the context of long-term disease management.

Adolescents represented a particularly vulnerable subgroup, with studies indicating increased rates of depression, anxiety, and body image dissatisfaction, especially among those with poor dietary adherence. These findings underscore the interaction between developmental stage, disease burden, and psychological outcomes.

3.6. Associations with Biological and Psychosocial Factors

Several studies identified associations between psychiatric symptoms and biological markers of disease activity, including serological indicators, nutritional deficiencies, and comorbid autoimmune conditions. Deficiencies in micronutrients and amino acids involved in

neurotransmitter synthesis were frequently reported, although direct causal relationships with psychiatric outcomes were inconsistent.

Psychosocial factors-such as perceived disease control, social support, daily obstacles related to the gluten-free diet, and quality of life-were strongly correlated with both depression and anxiety. Patients reporting greater difficulty adhering to dietary restrictions and greater perceived illness burden consistently demonstrated worse mental health outcomes.

3.7. Summary and Key Findings

Overall, the results of this review indicate that depression is a common and robustly supported psychiatric comorbidity in celiac disease, while evidence for anxiety is more heterogeneous and context-dependent. Psychiatric symptoms are influenced by disease status, age, dietary adherence, and a complex interplay of biological and psychosocial factors. These findings provide a foundation for the subsequent discussion of mechanisms, clinical implications, and directions for future research.

4. Discussion

The present review and meta-analytical synthesis confirms that psychiatric symptoms constitute a significant and clinically relevant component of celiac disease, extending far beyond its classical gastrointestinal manifestations. The findings indicate that depression, in particular, is consistently more prevalent among individuals with celiac disease than in the general population, whereas anxiety appears to be more variably expressed and strongly influenced by contextual and methodological factors. These results reinforce the conceptualization of celiac disease as a multisystem disorder in which psychological morbidity is an integral part of the disease burden.

Among the psychiatric manifestations examined, depression emerged as the most robustly supported comorbidity of celiac disease. Across clinical cohorts, population-based studies, and meta-analyses, individuals with CD demonstrated a higher prevalence and severity of depressive symptoms, particularly in the untreated or newly diagnosed stages of the disease. The consistency of these findings across age groups suggests that depression may represent a core feature of CD-related morbidity rather than a coincidental association.

Several mechanisms may underlie this relationship. Chronic intestinal inflammation and villous atrophy can lead to malabsorption of nutrients essential for central nervous system functioning, including tryptophan, folate, vitamin B12, iron, and omega-3 fatty acids. Impaired tryptophan availability, in particular, has been hypothesized to reduce central serotonin synthesis, thereby contributing to depressive symptomatology. Additionally, immune-mediated mechanisms-such as cytokine-induced neuroinflammation and activation of the hypothalamic-pituitary-adrenal axis-may further exacerbate mood disturbances. These biological pathways are not mutually exclusive and likely interact with psychosocial stressors to produce depressive symptoms in susceptible individuals.

In contrast to depression, the relationship between anxiety and celiac disease appears less consistent. While numerous clinical studies report elevated anxiety levels, particularly among women and adolescents, meta-analytical evidence suggests that anxiety in CD may not be significantly higher than in other chronic medical conditions. This finding supports the hypothesis that anxiety may reflect a nonspecific psychological response to chronic illness, uncertainty, and perceived lack of control rather than a CD-specific pathophysiological process.

Nevertheless, anxiety in celiac disease should not be underestimated. The requirement for strict, lifelong dietary vigilance can foster heightened health-related anxiety, fear of accidental gluten exposure, and social avoidance. In some patients, particularly those with high levels of conscientiousness or perfectionism, strict dietary adherence may paradoxically increase anxiety rather than alleviate it. These observations underscore the importance of distinguishing between anxiety driven by biological disease mechanisms and anxiety arising from psychosocial and behavioral demands associated with disease management.

The gluten-free diet remains the cornerstone of celiac disease treatment and plays a complex role in shaping psychiatric outcomes. The reviewed literature suggests that initiation of a GFD is often accompanied by partial improvement in depressive and anxiety symptoms, particularly during the first year of treatment. This improvement may be attributed to reduced intestinal inflammation, correction of nutritional deficiencies, and relief of somatic symptoms.

However, the persistence of psychiatric symptoms in a substantial subset of patients despite long-term dietary adherence highlights the limitations of diet-only approaches. In adults, especially those with delayed diagnosis or longstanding disease, psychological morbidity may become entrenched and less responsive to dietary intervention alone. Moreover, the GFD itself may introduce new stressors, including social restrictions, financial burden, and constant monitoring of food intake, which can negatively affect mental well-being. These findings suggest that while the GFD is necessary for intestinal healing, it is not sufficient to address the full spectrum of psychological consequences associated with celiac disease.

Age emerged as a critical moderating factor in psychiatric outcomes. In children and adolescents, psychiatric symptoms-particularly depressive and behavioral disturbances-often precede diagnosis and show greater improvement following dietary treatment. This pattern may reflect greater neuroplasticity, shorter disease duration, and more comprehensive family support in pediatric populations.

Adolescence, however, represents a particularly vulnerable developmental period. Studies consistently report elevated rates of depression, anxiety, and body image dissatisfaction in adolescents with celiac disease, especially among those struggling with dietary adherence. The interaction between developmental challenges, peer relationships, and the constraints of a gluten-free diet may amplify psychological distress in this group. These findings emphasize the need for age-specific screening and interventions tailored to developmental stage.

Psychosocial variables, including perceived disease control, social support, and daily obstacles related to dietary management, were strongly associated with psychiatric outcomes across studies. Poor quality of life, rather than objective disease severity alone, appears to be a key determinant of mental health in celiac disease. Patients who perceive their illness as uncontrollable or socially limiting are more likely to experience depression and anxiety, regardless of serological or histological disease markers.

This observation aligns with broader models of chronic illness adaptation, in which subjective illness perception and coping strategies play a central role in psychological adjustment. Accordingly, interventions aimed at improving mental health in CD should extend beyond medical and dietary management to include psychoeducation, psychological support, and strategies to enhance coping and resilience.

The findings of this review have important implications for clinical practice. Routine screening for depressive and anxiety symptoms should be considered an integral part of celiac disease management, particularly at diagnosis and during follow-up. Multidisciplinary care models involving gastroenterologists, dietitians, psychologists, and mental health professionals may be most effective in addressing the complex interplay between physical and psychological health in CD.

Future research should prioritize longitudinal designs to clarify causal relationships between celiac disease activity, dietary adherence, and psychiatric outcomes. Standardization of

psychiatric assessment tools and greater attention to confounding variables-such as comorbid autoimmune conditions, socioeconomic status, and physical activity-are also needed. Importantly, interventional studies evaluating combined dietary and psychological interventions may offer valuable insights into optimizing mental health outcomes for individuals with celiac disease.

In summary, psychiatric symptoms, particularly depression, are a prevalent and meaningful component of celiac disease that warrants systematic attention. Addressing psychological morbidity alongside intestinal pathology is essential for improving overall quality of life and long-term outcomes in this population.

5. Conclusions

Psychiatric symptoms constitute a significant and clinically important aspect of celiac disease, extending beyond its traditional characterization as a gastrointestinal disorder. The evidence synthesized in this review demonstrates that depression is a common and consistently reported comorbidity in both adult and pediatric populations with celiac disease, while anxiety, although prevalent in many clinical settings, appears to be more heterogeneous and strongly influenced by psychosocial and contextual factors.

The findings indicate that psychiatric symptoms are most pronounced in untreated or newly diagnosed individuals, supporting the role of active disease processes and systemic inflammation in the development of mood disturbances. Although adherence to a gluten-free diet is associated with partial improvement in depressive and anxiety symptoms, dietary treatment alone does not fully eliminate psychological morbidity in a substantial proportion of patients. Persistent psychiatric symptoms despite long-term dietary adherence highlight the limitations of a purely biomedical approach to disease management.

Both biological and psychosocial mechanisms contribute to the observed psychiatric burden in celiac disease. Nutritional deficiencies, immune-mediated neuroinflammation, and gut–brain axis dysregulation interact with disease-related stress, social restrictions, and perceived loss of control imposed by lifelong dietary treatment. Age-specific patterns further suggest that children and adolescents may benefit more rapidly from dietary intervention, whereas adults-particularly those with delayed diagnosis-are at increased risk of persistent psychological distress.

These conclusions underscore the necessity of a multidisciplinary model of care in celiac disease that integrates routine mental health screening, psychological support, and individualized dietary counseling alongside standard gastroenterological management. Early identification and targeted treatment of psychiatric symptoms may improve not only mental well-being but also dietary adherence, quality of life, and long-term disease outcomes.

Future research should focus on longitudinal and interventional studies to clarify causal pathways and to evaluate combined nutritional and psychological treatment strategies. Standardized assessment of psychiatric outcomes and greater attention to patient-centered measures are essential to advancing a holistic understanding of celiac disease and optimizing care for affected individuals.

Disclosure

Author's contribution

Conceptualization: [JM], [KWoj]
Methodology: [KW], [JM], [WW]
Check: [JM], [MP], [NK]
Investigation: [JB, JM], [WW]
Data curation: [AB], [KWoj], [MP], [JN]
Writing - rough preparation: [JM], [KWoj], [TS]
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