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Clinical manifestations, comorbidities, and therapeutic approaches of celiac disease in pediatrics: A systematic review

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ABSTRACT

Objective: The general objective of the present study is to analyze the scientific production on Celiac Disease, seeking to identify the main clinical manifestations, as well as the main comorbidities and the main methods used in the treatment of this pathology. Methodology: It is a systematic review focused on understanding the main aspects of Celiac Disease. The research was guided by the question: "What are the clinical manifestations, associated diseases and management of celiac disease in pediatric patients, based on the evidence available in the scientific literature?". To find answers, searches were performed in the PubMed database using three descriptors combined with the Boolean term "AND". This resulted in 268 articles. 17 articles were selected to compose the collection. Results: Celiac Disease (CD) is an immune-mediated condition that affects the gastrointestinal tract and can cause several symptoms, including extraintestinal manifestations. Diagnosis involves serological testing and biopsies, with gluten removal being the only effective treatment. Strict adherence to the gluten-free diet is crucial for recovery, but it can vary between patients, impacting long-term health. Conclusion: CD is associated with other autoimmune and genetic conditions, requiring regular monitoring and ongoing support to ensure the well-being of patients.

Keywords: Celiac Disease, Pediatrics, Clinical Manifestations.

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INTRODUCTION

Celiac disease is an immune-mediated systemic disease triggered by the ingestion of gluten and prolamins in genetically predisposed individuals, characterized by the presence of various combinations of small bowel damage, presence of celiac disease-specific antibodies, human leukocyte antigen (HLA)-DQ2 or HLA-DQ8, and gluten-dependent clinical manifestations. Gluten refers to insoluble proteins from cereals, including prolamins found in wheat (gliadins), rye (secalines), barley (hordein), and oats (avenins). (HOUMICH; ADMOU, 2021) (SAHIN, 2021).

It is estimated that up to 40% of the general population carries the susceptibility genes, but the prevalence of celiac disease is only about 1% of the general population. The average age at the time of diagnosis is school, which varies between 6 and 9 years, but the disease can occur at any time, from early childhood to old age. The seroprevalence of celiac disease and the prevalence of biopsy-proven celiac disease in the world are 1.4% and 0.7%, respectively. Its prevalence varies depending on geographic and ethnic variations. The highest prevalence is in Europe (0.8%) and Oceania (0.8%), and the lowest prevalence is in South America (0.4%). The prevalence of biopsy-proven celiac disease was 1.5 times higher in women than in men, and the incidence of celiac disease is twice as high in children compared to adults (SAHIN, 2021) (LUPU et al., 2023). The reason for this difference may be genetic factors [human leukocyte antigen (HLA) and non-HLA genes], environmental factors such as wheat consumption, age at gluten intake, gastrointestinal infections, proton pump inhibitor and antibiotic use, and the rate of cesarean section. (SAHIN, 2021) (TORUN et al., 2021).

Celiac disease is more prevalent in so-called high-risk groups, such as type 1 diabetes (1–12%); autoimmune thyroid disease (2–6%); Down syndrome (2–6%); autoimmune hepatitis (3–7%), Turner syndrome (4–5%); first-degree relatives with celiac disease (10–20%); individuals with iron deficiency anemia (3–15%); patients with osteoporosis (1–3%), and many other clinical conditions. In addition, the incidence of celiac disease has increased significantly over the past 30 years, from 2–3 to approximately 9–13 new cases per 100,000 population per year. This probably reflects a fortuitous discovery of non-classical, asymptomatic forms. (HOUMICH; ADMOU, 2021)

Celiac disease usually occurs in genetically predisposed individuals who respond to unknown environmental factors with an immune response that is subsequently triggered by gluten ingestion. Environmental factors, such as the duration of gluten exposure, play important roles in the development of celiac disease. The key elements of celiac disease, an autoimmune disease, are the genetic genotypes HLA-DQ2 and HLA-DQ8, environmental factors (gluten intake), and autoantigen for tissue transglutaminase (tTG), which are known to play an important role in pathogenesis. In addition to genetic susceptibility and gluten exposure, loss of gut barrier function, gluten-induced innate pro-inflammatory immune response, inadequate adaptive immune response, and imbalanced

gut microbiome appear to be components of celiac disease autoimmunity. More than 99% of celiac patients have HLA-DQ2 or HLA-DQ8 compared to 40% in the general population (SAHIN, 2021) (SUN et al., 2024).

This systematic review article aims to compile and analyze the scientific evidence on the clinical manifestations and management of Celiac Disease, as well as its main complications. The objective is to provide a comprehensive and up-to-date view, which synthesizes existing knowledge and identifies gaps in research, guiding future investigations and clinical practices. In-depth analysis of the evidence is intended to be a useful resource for healthcare professionals, researchers, and academics, contributing to the improvement of diagnostic and therapeutic approaches

METHODOLOGY

This is a systematic review that seeks to understand the main aspects of Celiac Disease in pediatric patients, as well as to demonstrate the main diseases associated with the condition. For the development of this research, a guiding question was elaborated through the PVO (population, variable and objective) strategy: "What are the clinical manifestations, associated diseases and management of celiac disease in pediatric patients, based on the evidence available in the scientific literature?"

The searches were carried out through searches in the PubMed Central (PMC) databases. Four descriptors were used in combination with the Boolean term "AND": Celiac Disease, Pediatrics, Clinical Diagnosis, and Signs and Symptoms. The search strategy used in the PMC database was: (Celiac Disease) AND (Pediatrics); (Celiac Disease) AND (Pediatrics) AND (Clinical Diagnosis) and (Celiac Disease) AND (Pediatrics) AND (Signs and Symptoms) . From this search, 268 articles were found, which were later submitted to the selection criteria. The inclusion criteria were: articles in English, Portuguese and Spanish; published in the period from 2019 to 2024 and that addressed the themes proposed for this research, in addition, review, observational and experimental studies, made available in full. The exclusion criteria were: duplicate articles, available in the form of abstracts, that did not directly address the proposal studied and that did not meet the other inclusion criteria.

After associating the descriptors used in the searched databases, a total of 268 articles were found. After applying the inclusion and exclusion criteria, 24 articles were selected from the PubMed database, and a total of 17 studies were used to compose the collection.

DISCUSSION

Celiac disease (CD) is an immune-mediated systemic disease, characterized by a variable pattern of clinical manifestations in the gastrointestinal and extraintestinal tract, but is clearly defined

by the presence of a gluten-dependent atrophic enteropathy (small intestine), along with a consistent serological panel through positivity for anti-tissue transglutaminase antibody and/or antiendomysial antibody. CD is involved in infection of the gastrointestinal tract, mainly in the small intestine. The persistent inflammatory reaction is triggered by the consumption of gluten-containing products (such as wheat, barley, and rye) and disappears when gluten is removed from the diet (PODDIGHE; KUSHUGULOVA, 2021) (JAFARI et al., 2024).

Gluten, as already mentioned, represents another necessary condition for the induction of CD. As a protein blend, the main components of gluten are gliadin and glutein. Gliadin is the main triggering antigen for CD through its components glutamine and proline. When these proline-rich peptides reach the small intestine, they have a longer degradation period, increasing the chance of activating an immune response. Once innate and adaptive responses are activated, the consequences are the infiltration of inflammatory cells and the promotion of cytotoxic CD8 T cells. In this way, atrophy of the mucosal villi, hyperplasia of the crypts, and dysfunction of the intestinal barrier arise. These changes imply the promotion of pathogenic bacteria, increased translocation capacity, and intestinal permeability, pathognomonic characteristics of celiac disease (LUPU et al., 2023) (LUPU et al., 2024).

CD is a complex disease triggered by several factors, including genetic and environmental elements. In people with genetic predisposition, for example, the presence of HLA genes such as HLA-DQ2 or HLA-DQ8, when these individuals are exposed to gluten and environmental elements, this causes the activation of their innate and adaptive immune responses. Genetic origin plays a crucial role in the predisposition to CD. The HLA-DQ2 haplotype (DQA10501-DQB10201) is present in most individuals affected by CD (90%), while the HLA-DQ8 haplotype (DQA10301-DQB10302) is found in 5% of these cases, which carry at least one of the two DQ2 alleles, especially DQB1*0201. Both haplotypes are involved in the development of CD and are expressed on the surface of APCs. These cells have a strong affinity for gluten-derived deamidated peptides, which bind to and present to CD4 T cells in the suburothelium, initiating the inflammatory cascade, which is a function of CD. Autoantibodies against TG2, specifically anti-TG2 and anti-EMA, are responsible for gluten deamination in CD patients. However, the most important alteration is intestinal damage, often characterized by villous atrophy, a scientific feature in most cases of CD (JAFARI et al., 2024).

Regarding the factors that can precipitate the occurrence of autoimmunity and celiac disease, it is evident that there is an increase in their risk proportional to each gram of gluten consumed per day. Another variable is represented by the type of birth, a physiological process that can leave marks on the child's future course, increasing the incidence of certain diseases (respiratory tract infections, asthma, obesity, autism spectrum disorders, attention deficits or delays in neuropsychic

development). This aspect is usually attributed to an incomplete development of the infant microbiota in babies born by cesarean section. To this are added particular aspects of the first years of life. However, data regarding the impact of cesarean section, breastfeeding, or the age of introduction of gluten into the diet on the increased risk of CD are contradictory (LUPU et al., 2024).

There is growing evidence that "Western" diets (high in animal protein and processed foods) promote inflammation through direct or indirect modulation of the immune system, while a "prudent" or "Mediterranean" diet (rich in vegetables and grains, with low consumption of processed foods and added sugars) has demonstrated anti-inflammatory properties, which may extend to a protective effect on the development of CD in children (CHANG etal., 2022).

Symptoms usually occur in children after ingestion of gluten-containing grains between 4 and 24 months. There may be a delay or latent period between eating gluten and the onset of symptoms. The term "classic CD" is used when symptoms associated with malabsorption, such as diarrhea, bloating, weight loss, or growth failure, are present, while "non-classic CD" is employed for all other symptoms (CHANG et al., 2022). Common extraintestinal manifestations are growth retardation, short stature, chronic anemia, osteopenia, osteoporosis, delayed puberty, tooth enamel defect, irritability, chronic fatigue, neuropathy, arthritis, arthralgia, amenorrhea, and increased liver enzymes (SAHIN, 2021).

Symptoms are usually different in infants and in older children. The classic triad of CD symptoms, such as diarrhea, distension, and abdominal pain, is more frequent in younger children, while with increasing age, atypical symptoms become more common. If diagnosis is delayed, growth delays, irritability, and severe malnutrition may be observed. Gastrointestinal symptoms such as diarrhea, nausea, vomiting, abdominal pain, bloating, weight loss, and constipation can occur in older children, depending on the amount of gluten intake. Gastrointestinal manifestations, such as diarrhea, are observed in approximately 50% of patients with celiac disease (SAHIN, 2021) (SCAPATICCI et al., 2023).

Clinical manifestations may be mild or absent (with only a slight elevation of transaminases) or may be characterized by extra-intestinal involvement of any part of the body (alopecia, dermatitis herpetiformis), including the nervous system. Extraintestinal findings are seen in up to 60% of pediatric celiac patients. Short stature is the most common finding in children. It has been reported that 10%-47.5% of pediatric celiac patients have short stature at the time of diagnosis. 19% to 59% of non-endocrinological causes of short stature are reported as celiac disease. Starting a gluten-free diet in the initial period causes rapid weight growth and regain, especially in the first 6 months. The target height is usually reached within 3 years of diagnosis. If the target height is not reached despite a strict gluten-free diet, an endocrinological evaluation should be done to rule out growth hormone deficiency (SAHIN, 2021) (SABINO et al., 2020).

Hypogonadism in girls and delayed puberty in boys due to androgen resistance are common findings in undiagnosed or untreated pediatric celiac patients. Delayed puberty is seen in 10%-20% of celiac patients. Generally, the development of puberty occurs within 6 to 8 months of starting a gluten-free diet. If delayed puberty persists, the patient should be referred to pediatric endocrinology for further evaluation of other reproductive system disorders (SAHIN, 2021).

Dermatitis herpetiformis (HD) is a chronic, pruritic, gluten-induced skin condition characterized by granular subepidermal deposits of IgA, leading mainly to papulovesicular lesions. Links between CD and HD have emerged in recent decades: the disappearance of the rash on a gluten-free diet (GID), the occurrence of both conditions within families, and the overlap of human leukocyte antigen (HLA). Approximately 85% of HD patients of Caucasian origin are carriers of HLA-DQ2, while most others are carriers of HLA-DQ8. Although HD is not uncommon among adolescents, it is rarely seen before puberty, with most children diagnosed between the ages of 2 and 7 years. The clinical picture of HD is characterized by papulovesicular lesions and urticarial plaques, which itch intensely and are symmetrically distributed, typically affecting the extensor surfaces (elbows, knees, and buttocks). Because the lesions are strongly pruritic, typical vesicles are rarely apparent as they turn into excoriation. HD presents similarly in children and adults; however, children may present with unusual cutaneous findings such as solitary involvement, hemorrhagic lesions on the palms and soles, as well as deep dermal papules/nodules and facial lesions. Acral purpura and petechiae are a common finding among HD patients and may even indicate an early-stage disease: these hemorrhagic skin lesions mainly affect the fingers and toes and are called digital purpura (PERSECHINO et al., 2021).

The process of iron absorption develops mainly in the proximal duodenum. This portion of the intestine is normally destroyed in celiac disease (CD), resulting in a reduction in iron absorption and subsequent iron deficiency anemia (ADF). In fact, the most frequent extraintestinal manifestation (IBM) of CD is FAD, with a prevalence between 12 and 82% in patients with a new diagnosis of CD. 84% of pediatric celiac patients have been reported to make complete recovery from iron deficiency anemia with a strict gluten-free diet and iron supplementation therapy within 12-24 months (FREEMAN, 2015) (SAHIN, 2021).

The most common concomitant disease is type 1 DM, since it has genetic factors and pathogenic mechanisms common to celiac disease. HLA-DQ2 is present in approximately 90%-95% of celiac patients and in 50% of patients with type 1 DM, but HLA-DQ8 is detected in approximately 10% of celiac patients and in approximately 70% of patients with type 1 DM. In a systematic review, the prevalence of celiac disease in patients with type 1 DM was reported to be approximately six times higher than in the general population. The prevalence of celiac disease was reported to be 2.4% to 16.4% in children with type 1 DM. There is consensus on initial screening for celiac disease in

newly diagnosed DM patients, but it is unclear when and how often to screen for celiac disease and start a gluten-free diet in asymptomatic patients. It has been recommended that screening testing for CD be performed at the time of diagnosis of type 1 DM and every 2 years thereafter. In another review, it was recommended that children diagnosed with type 1 DM should be screened for celiac disease once a year for the first 5 years. In other studies, it has been recommended that screening serologic tests for celiac disease be performed within the first 2 years when diagnosis is made, then 5 years after diagnosis, and if there are any symptoms suggestive of CD. As 58%-85% of patients with type 1 DM diagnosed with CD are asymptomatic, early diagnosis of CD is very important to prevent long-term complications such as growth retardation, osteopenia, infertility, and malignancy (SAHIN, 2021).

There is good evidence that autoimmune thyroid diseases are associated with celiac disease. The prevalence of celiac disease in patients with autoimmune thyroid is found to be 3.0%-4.8%. There is a close relationship between Down syndrome and celiac disease. The prevalence of celiac disease in patients diagnosed with Down syndrome is reported to be 5% to 12%. The North American Society of Pediatric Gastroenterology, Hepatology, and Nutrition and the European Society of Pediatric Gastroenterology, Hepatology, and Nutrition (ESPGHAN) recommend screening tests for celiac disease in children with Down syndrome because of the increased risk of developing celiac disease. In a study conducted in 2020, involving 1,317 pediatric patients with Down syndrome aged 3 years and older, the prevalence of celiac disease was 9.8% in children with Down syndrome. If celiac disease screening testing is not performed, the diagnosis of celiac disease is neglected or delayed in 82% of patients with Down syndrome, thus causing increased morbidity (SAHIN, 2021).

With regard to Juvenile Idiopathic Arthritis (JIA), >2.5% of JIA patients were diagnosed with CD; however, the prevalence of CD in JIA patients may be even higher (>3–3.5%) due to several limitations of the study that could have underestimated the diagnosis of JIA to a variable extent. Therefore, serologic screening for CD in children affected by JIA could be recommended due to the increased prevalence of CD in these patients (compared to the general pediatric population) and because these JIA patients diagnosed with CD were mostly asymptomatic. However, more research is needed to establish a cost-effective approach in terms of frequency and modalities of CD screening during the follow-up of patients with JIA. On the other hand, at present, there is no evidence to support a periodic screening for CD in children affected by other rheumatic diseases (including pediatric systemic lupus erythematosus, juvenile dermatomyositis, and systemic sclerosis) (PODDIGHE et al., 2022).

Over the past 40 years, serology has become increasingly relevant for the diagnosis of celiac disease (CD). Prior to the mid-1980s, CD could only be diagnosed by clinical suspicion and

duodenal biopsy. Although the intestinal biopsy showing the typical flat mucosa picture is still considered the "gold standard" for diagnosing CD, antibody markers have radically changed the celiac world (VOLTA et al., 2023).

The diagnosis of CD begins gradually, from non-invasive to invasive, and the choice of method is made according to the individual risk of each patient. Biologically, serology includes endomysial antibodies (EMA), tissue transglutaminase (tTG), and deamidated gliadin peptide (DGP) assays, high-sensitivity and specificity tests (LUPU et al., 2024). In daily practice, when CD is suspected, symptomatic or not, or in high-risk individuals, the first line of screening is based on the detection of anti-TG2 IgA, followed, if positive, by AME, a highly specific marker, which improves the positive predictive value (PPV) of serological tests. In fact, the simultaneous positivity of multiple tests makes the diagnosis of CD very likely. In addition, a combination of anti-TG2 IgA with anti-TG2 IgG allows for the deletion of CD potentially concealed by IgA deficiency. In addition, the PPV of these tests in low-risk populations for CD depends on antibody titers. Low titers (less than three times the limit) in asymptomatic patients should be retested after 3 to 6 months on a gluten-rich diet before considering endoscopy and biopsies (HOUMICH; ADMOU, 2021).

Pathologic diagnosis is established or confirmed according to the modified Marsh-Oberhuber and Corazza-Villanacci classifications, with different scales based on intraepithelial lymphocyte count, crypt hyperplasia, and villous atrophy. To properly evaluate the histological abnormalities of CD according to commonly used criteria, it is recommended to correctly guide endoscopic sampling (four to six staged biopsies of the bulb and/or second duodenum) and repeat biopsy section levels. In fact, an imperfectly oriented sample can lead to misdiagnoses of 5% to 10%. In young children, endoscopy may show a different pattern, with a lower prevalence of atrophy, and there is a need for more biopsies to establish the diagnosis with certainty (FREEMAN, 2015). The introduction of serological tests associated with non-invasive methods of evaluation of the intestinal mucosa and the possibility of new non-invasive strategies are very promising for the screening and diagnosis of CD (HOUMICH; ADMOU, 2021).

The main histological criteria for CD include villous atrophy (VA) of varying degrees with increased number of intraepithelial lymphocytes (IEL). These two signs, although nonspecific, strongly suggest CD and are associated with crypt hyperplasia and increased chorionic cell density. However, VA and increased IEL can be associated with several pathologies. In addition, patients with isolated increased IEL with positive serological tests are considered potential candidates for CD as an asymptomatic latent form, whereas in most cases, the presence of solitary intraepithelial lymphocytosis does not correspond to CD. On the other hand, almost all VA associated with IEL, compensatory crypt hyperplasia, chorion hypercellularity (increased density of inflammatory cells

and IgA plasma cells) and positive serological tests correspond to silent forms of CD (HOUMICH; ADMOU, 2021).

In children with suspected CD, the current trend is non-systematic use of intestinal biopsy. Notably, the European Society of Paediatric Gastroenterology, Hepatology and Nutrition has proposed a biopsy-free approach in symptomatic children who meet the following four criteria: typical clinical signs, anti-TG2 10 times or more the upper limit of normal (ULN), positive EMA, and positive HLA DQ2 and/or DQ8. More recently, a group of experts has assumed that even asymptomatic children can be accurately diagnosed with CD without biopsy, but only on the basis of elevated anti-TG2 IgA titers (10 times or more the ULN), positive EMA tests in 2 blood samples (HOUMICH; ADMOU, 2021).

The immune response to vaccinations in celiac patients is of growing scientific interest. However, some aspects of the relationship between celiac disease (CD) and vaccines are still unclear. To date, there is no evidence to demonstrate any causal association between vaccines and the development of CD. Therefore, vaccines can be administered according to the modalities and schedules of the National Immunization Calendar of each country. The rotavirus vaccine is currently recommended for the general population and, according to some data, appears to reduce the risk of developing autoimmunity against CD in the first years of life. Regarding the hepatitis B virus, a booster dose of the vaccine is often required due to the low or missed rate of immune response in CD. In addition, the determination of hepatitis B antibody titers may be useful in newly diagnosed individuals with CD, regardless of age at diagnosis (PASSANISI et al., 2020).

The current treatment for CD is a strict gluten-free diet (GFD) throughout life, which achieves symptom remission within a few days or weeks and restoration of intestinal villi and immune homeostasis within a few months (MARTÍN-MASOT et al., 2023). Rapid improvement of clinical symptoms is seen within 2 to 4 weeks in children. Serologic and histologic responses are slower compared to clinical symptoms. Although histological response in children is observed within 2 years by a rate of 95%, this rate is 60% in adults (SAHIN, 2021).

The amount of tolerable gluten varies from patient to patient. As little as 50 mg of gluten, present in some amounts of breadcrumbs or a small piece of cake or traces of contamination, can cause symptoms and/or enteropathy in asymptomatic patients. A gluten intake of less than 10 mg/day is unlikely to cause significant histological abnormalities. Adherence to the gluten-free diet has some disadvantages; Negative impact on quality of life, psychological problems, unintentional gluten contamination, possible vitamin and mineral deficiencies, metabolic syndrome, increased cardiovascular risk and severe constipation. Adherence to the gluten-free diet is better in children diagnosed with CD at an early age and in those who continue to have regular follow-up. It is lower in adolescents compared to adults (SAHIN, 2021).

After 18 months of close monitoring of GID, the celiac has most of the parameters equivalent to those of a healthy child. This is an important fact, but even so, the usual delay in diagnosis (due to its difficulty), combined with the time for stabilization of the disease, is too long, and during this period complications may develop that will result in sequelae ranging from mild (for example, permanent short stature, tooth enamel failure and psychiatric problems) to serious, such as tumors, in the long term. The fact is that GID seems to play an important role in the pathogenesis of tumor development, since some studies have described a greater development of tumors the later the diagnosis is made and in patients who did not follow GID. Thus, untreated CD is mainly associated with T-cell lymphoma (T-cell lymphoma) and adenocarcinoma of the small intestine, although a higher incidence of non-Hodgkin's lymphoma and colorectal cancer has also been described (MARTÍN-MASOT et al., 2023).

Patients with celiac disease should be followed up 6 months after diagnosis and every 6 months in terms of symptom improvement, adherence to the gluten-free diet, quality of life, and progressive normalization of antibodies associated with celiac disease. Screening tests should be done in terms of autoimmune thyroid disease. A control duodenal biopsy is not necessary after a gluten-free diet. However, if there is a partial or no response to the gluten-free diet, careful examination should be done to detect unintentional gluten contamination or poor adherence to the gluten-free diet. If the response to a strict gluten-free diet is poor, duodenal biopsy can be performed (SAHIN, 2021).

The best marker of proper follow-up and management is a decline in antibody levels and a return of antibody levels to normal at follow-up. The presence of persistent positive antibodies usually indicates ongoing intestinal damage and gluten exposure. Serological follow-up should be done within 6 months and 12 months of diagnosis and then once a year. The tTG-IgA test is reported to be the best test at follow-up. The median time to return to normal tTG test levels in patients with strict adherence to the gluten-free diet has been shown to be 1 year (SAHIN, 2021).

CONCLUSION

Celiac Disease (CD) is a complex, multifaceted condition with an immune-mediated basis that affects the gastrointestinal tract and can manifest in a wide range of extraintestinal symptoms. The identification of CD involves a combination of genetic factors, gluten exposure, and immune responses that result in intestinal villous atrophy and changes in the intestinal barrier. Diagnosis is based on a combination of serological tests and biopsies, with anti-tissue transglutaminase and anti-endomysium antibodies being the main markers at screening.

The relationship between diet and CD is crucial, with gluten removal being the only effective form of treatment. Strict adherence to the gluten-free diet is essential for the remission of symptoms

and recovery of intestinal function. However, the impact of the diet and adherence to it can vary between patients, with potential long-term consequences in case of late diagnosis or poor adherence. It is essential that CD patients are monitored regularly to ensure adherence to the diet, assess the evolution of symptoms, and prevent complications associated with the untreated disease, such as increased risk of cancer.

In addition, CD is often associated with other autoimmune and genetic conditions, and screening for these conditions should be considered in the follow-up of celiac patients. The continuous evolution of diagnostic and treatment strategies, combined with patient education and support, are vital for the effective management of CD and the improvement of the quality of life of those affected.

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