



## Major Considerations of Celiac Disease: A Narrative Review

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**Abstract:** Celiac disease (CD) is an autoimmune disease. Whoever has it cannot eat foods that have gluten in their composition. The only treatment available is a diet in which all products containing gluten are removed from the dietary routine of patients with CD, which requires that their patients have determination. It is of utmost importance that the maximum amount of information is provided to the patient, so that the patient has a wide awareness of the conditions and limitations to be respected, as well as of the possible harmful changes to health caused by the non-adherence of the gluten-free diet.

**Keywords:** Celiac disease, Gluten, Treatment.

### Introduction

Celiac disease (CD) has a global prevalence of about 1% [1]. It is defined as a systemic autoimmune disease triggered by the ingestion of dietary proteins present in wheat, barley, and rye, known as gluten [2,3]. Affected individuals are genetically predisposed and have autoantigens, such as tissue transglutaminase, and HLA class II genes DQ2 and/or DQ8, inducing an autoimmune response and lesions in the small intestine mucosa [3]. This also directly impacts the intestinal microbiota [4].

In this regard, studies have found a relationship between the reduced number of beneficial bacteria, such as Bifidobacterium and Lactobacillus, and the presence of CD [4]. Still, other symptoms may be related to the gastrointestinal tract, such as diarrhea, vomiting and abdominal pain, anemia, mental abnormalities, and reduced bone density [5,6]. In this context, an important treatment to stabilize the chronic inflammatory condition of CD is through the administration of prebiotics and probiotics [7-9], enabling the reduction of inflammatory cytokines, such as TNF- $\alpha$ , IFN-gamma, and IL-2, and increase in anti-inflammatory cytokines, such as IL-10 [10,11].

Still, studies show that a gluten-free diet can restore the intestinal composition of bacteria in CD. In addition, patients with CD can continue to manifest gastrointestinal symptoms even under this therapy, as has been observed in children and women [8]. In addition, 40-50% of patients still have long-term

intestinal inflammation [9]. In this scenario and according to historical bases, DC originated at the time when primitive individuals began to show a change in their routine, adopting a way of life/food not only as a hunter but also as a collector. Along with this new agricultural food style, a sedentary lifestyle came. It is said that this occurred around 10,000 BC and during this period there was large cultivation of cereals [12].

Still, the same author, Shils (2009), informs that during the process of alcoholic gluten extraction, there is also the production of a soluble fraction called glutenins. It contains prolamines and an insoluble fraction. Both are thought to be highly toxic to the intestinal mucosa of celiac patients. The author points out that there are non-toxic cereals, such as rice and corn, which contain a low concentration of prolamines. When CD is diagnosed early, it can help prevent other possible complications that are associated with the disease [12]. In addition, Shils (2009) argues that the production of antibodies is probably linked to an increase in the permeability of the intestinal mucosa identified in celiac disease. Also, according to the author, there is a layer of very sensitive connective tissue that surrounds the entire striated intestinal musculature, such a layer is called endomysium. And, from a study, anti endomysial antibodies were found in more than 95% of the celiac patients analyzed [12].

Also, Melo (2005) understands celiac disease as an autoimmune disease of the small intestine, with gluten as the main responsible for the pathogenesis, with the tissue transglutaminase enzyme as the role of

the autoantigen. Also, according to the author, this pathology is linked to several other autoimmune diseases, such as, for example, Systemic Lupus Erythematosus, Type 1 Diabetes Mellitus, Rheumatoid Arthritis, Autoimmune Thyroid Diseases and Sjögren's Syndrome [13].

For Sdepanian (2001) the main characteristic of celiac disease is the permanent intolerance to the consumption of any food that has gluten in its composition. Certain cereals such as barley, wheat, malt, oats, among others, can be mentioned as examples of foods that contain gluten [14]. And when someone intolerant of this component ingests it, an inflammatory process begins in the body where the mucosa of the proximal small intestine is affected, thus causing a subtotal or total atrophy of the intestinal villi, making it difficult for nutrients to be absorbed. of the foods that are eaten, in addition to some other symptoms.

Araújo (2010) places gluten as a prosthetic component of wheat species, which is responsible for the structure of the food and consists of some fractions of glutenin and gliadin. In wheat flour, this represents 85% of the prosthetic fraction. The author points out that anyone who is found to be celiac should ingest a maximum of 10mg of gliadin a day [15]. For Gama and Silva (2010), when an individual is presenting with chronic diarrhea, flatulence, early-onset osteoporosis, hypocalcemia, abdominal distension, iron deficiency anemia, elevated transaminases, deficiency of folic acid and fat-soluble vitamins, and some first-rate family member or second degree that contains celiac disease, then celiac disease should be mentioned as a probable diagnosis [16].

Also, Gama and Silva (2010) report that gluten proteins have resistance to digestive enzymes, which results in peptide derivatives that can provoke an immunogenic response in celiac patients. The authors also point out that the manifestations from the inflammatory process in celiac patients can negatively affect several organs such as the liver, the gastrointestinal tract, the reproductive, nervous, and endocrine systems, bone, and skin [16].

In addition, Sdepanian et al. (2001) state that to diagnose celiac disease, "it is essential to perform a biopsy of the small intestine" [17]. And, for Ober Huber (2000), even if the diagnosis can be considered based on clinical manifestations, its confirmation will depend on the demonstration of the histopathological changes identified through biopsies of the small intestine, this being the standard procedure for defining the diagnosis

[18]. Although there is a great contribution of serological markers when identifying who should undergo a biopsy of the small intestine, it is essential to perform the histopathological exam.

Therefore, the present study had as its main objective to understand celiac disease, its appearance, and what it may cause in the organism of those who have it. In addition, he presented ways to live with the disease daily from a thoughtful diet.

## Methods

### Study Design

The rules of the Systematic Review-PRISMA Platform (Transparent reporting of systematic reviews and meta-analysis- [HTTP://www.prismastatement.org/](http://www.prismastatement.org/)) were followed [19].

### Data sources and research strategy

The search strategies for this systematic review were based on the keywords (MeSH Terms): 'Celiac disease; Gluten; Gut microbiota; Treatment'. The research was carried out in the SCOPUS, PUBMED, and SCIENCE DIRECT, including the National Institutes of Health RePORTER Grant database and clinical trial records. Also, a combination of the keywords with the booleans "OR", AND and the operator "NOT" were used to target the scientific articles of interest. The title and abstracts were examined under all conditions.

### Study Quality and Bias Risk

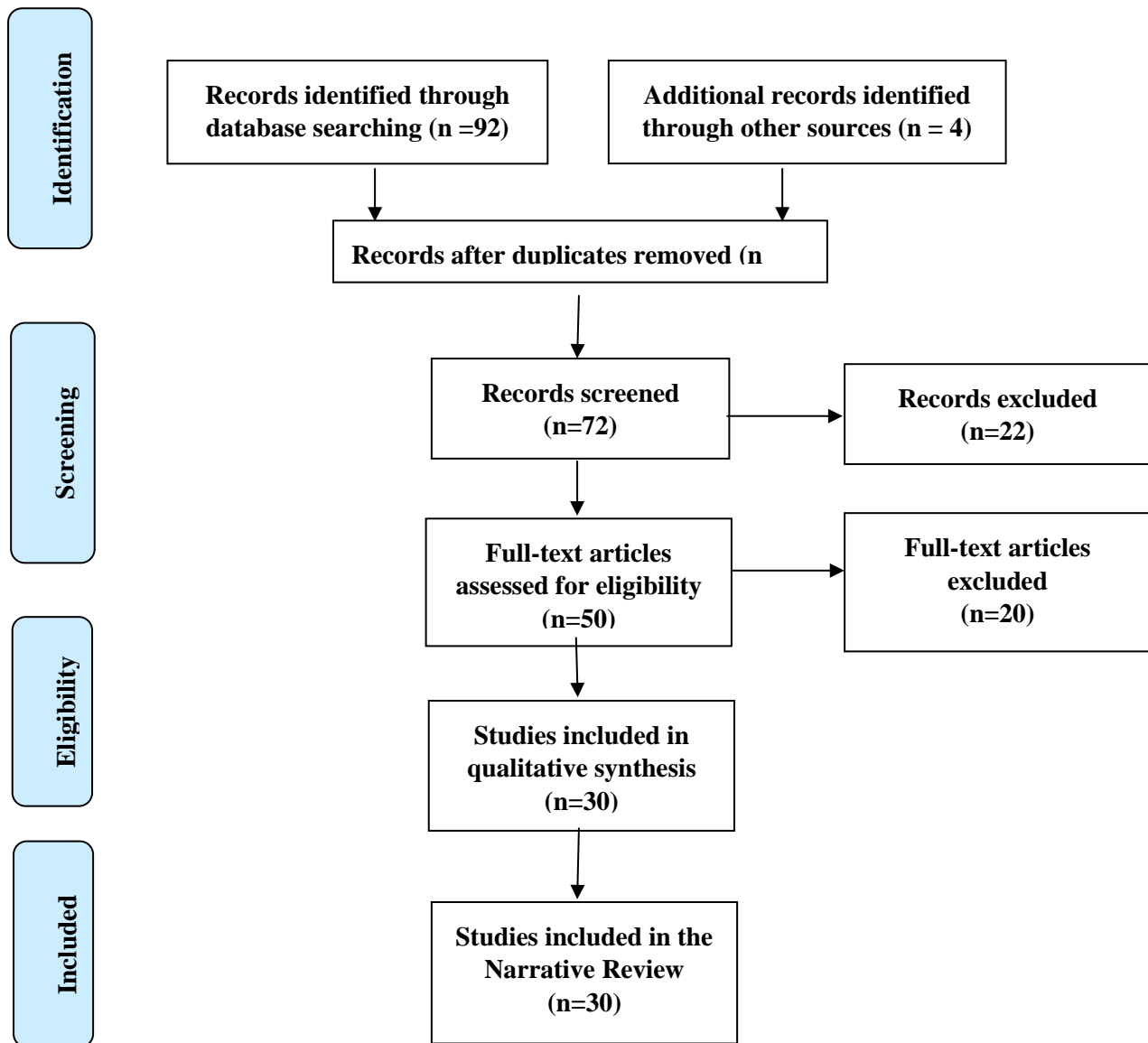
The quality of the studies was based on the GRADE instrument [20] and the risk of bias was analyzed according to the Cochrane instrument [21].

## Results and Discussion

A total of 96 studies were found that were submitted to the eligibility analysis, and, after that, 30 studies of high to medium quality and with risks of bias were selected that do not compromise the scientific basis of the studies (Figure 1).

### Celiac Disease and Gluten-Free Cereals in History

Wheat is estimated to have appeared more than ten thousand years ago in the Mesopotamian region.



**Figure 1.** Study Eligibility

informs that from archaeological findings and studies carried out, it is estimated that wheat was the second grain cultivated. The first being barley [22].

It is believed that the emergence of grains was a watershed at that time, where man was able to abandon hunting activities and start devoting himself to the development of Western civilization, remaining fixed in a certain village and helping in the construction of the city.

Thus, creating professions, sciences, arts, among other things. Everything from the reserves made from the stored seeds. Wheat is currently used in conjunction with rice as one of the most consumed cereals worldwide [23]. Still according to the author, barley is the oldest known cereal, being considered one

of the main sources of food for both humans and animals. Representing the fifth largest harvest. Trans (1856) reports that there are some data related to celiac disease dating from the 1st century AD [24]. However, it was only in 1988 that the disease was described. Samuel Gee being responsible for this. He described the disease as "celiac disease", referring to "chronic indigestion found in people of all ages, especially in children between 1 and 5 years old". He also defended the idea that the treatment of the then disease should work based on a manipulated diet. However, even though he was responsible for describing the disease where he limited it to children up to 5 years old, he was unable to identify specifically what exactly was the cause/responsible for the symptoms presented.

Mendonza (2005) says that many diets were prescribed and tested to treat the disease, especially the banana diet. Bergehenegouwen (1993) points to the period of the second world war as a period in which the negative effects due to the ingestion of some types of cereals ended up being related to celiac disease [25]. It was in 1950 that a Celiac Disease Association was created. The Association was created by a Dutch pediatrician known as Willem Dicke. It was he who discovered gluten as responsible for the felt effects, proposing a gluten-free diet for the treatment of the disease.

When World War II ended, Dick and Van de Kamer were able to confirm their suspicions about eating gluten-free cereals with symptoms linked to the disease. This confirmation was based on a study in which the weight and fat found in the feces of celiac children who had a gluten-free diet were analyzed, thus being able to calculate the malabsorption of nutrients. With these studies, it was possible to demonstrate what the consumption of wheat, oats, barley, and rye was capable of causing in the organism of those who had celiac disease. In addition to finding a solution to the problem by excluding the intake of these items daily [25]. It was shown that gluten was the main responsible for the damage in the intestine of those who had the disease, the first intestinal biopsies of celiac patients who died.

### The Definition of Celiac Disease

Celiac disease is seen as a disorder with a wide spectrum of clinical manifestations, which may be intestinal or extra-intestinal. Varying to gravity. As a result of the organism's sensitivity to the gluten ingested by individuals who have a genetic predisposition, consequently having an immunological reaction and generating inflammation in the small intestine, which may suffer and atrophy [26]. Still, gluten is a polypeptide that is part of wheat, oats, barley, and rye. Having alcohol-soluble protein fractions known as prolamines. Prolamines being a toxic item for all celiacs, suffering a difference according to the cereal [25].

In this sense, the accuracy of the gliadin toxicity in the intestine of those who have the celiac disease has already been proven. However, when it comes to oats, there are different speculations regarding their toxic fraction. Then needing more in-depth studies to support such a theory. However, while there is no exact definition on this subject, the exclusion of oats is still recommended for celiac patients. The author also points out that, it is not known exactly why the mechanism is

damaged by gluten, but it is believed to be a genetic, environmental, and immunological cause. Where the intake of these foods by those with a predisposition can cause a highly serious injury to the intestinal mucus, leading to deficiencies due to the nutrients being absorbed by different parts of the gastrointestinal tract [24-26].

### Genetic Factors

CD is associated with the system of human histocompatibility antigens (HLA). HLA locus is found on chromosome 6. More specifically in the 6p21.3 region. The genes in this system are lately relevant to the emergence of autoimmune diseases as a whole. This complex has genes that are organized into different classes. However, to talk about this part, the focus will be on class II. In this class are the products of the genes of the HLA-D group, which consists of HLA-DP, DQ, and DR. Such molecules work linked to antigenic peptides, presenting themselves to T cells. Some studies have been carried out for some years, and these have linked the appearance of celiac disease with specific DQ alleles, these being named HLA-DQ2 and DQ8 [27].

After some research, Stepniak, and Koning (2006) [28] point out that 95% of the cases monitored, there is an association with the HLA-DQ2 allele. And, HLA-DQ8 is associated with the remaining 5%. To identify these genes it is necessary to carry out a genetic test. Although this test is not 100% accurate to the diagnosis, it is possible to evaluate from it the imminent risk of the appearance of celiac disease, considering that it is possible to detect the presence of the alleles in question.

### Environmental Factors

Regarding environmental factors, gluten is considered the main etiological agent. This being a protein made up of different peptides. Glutenin and prolamines can be found in a wide variety of cereals, such as rye, barley, and wheat. These are the peptides that have the greatest impact when it comes to the development of celiac disease. In the group of prolamines, avenin can be found in oats. Gliadin in wheat. Secaline in the rye. Hordein in barley. Zein in maize [29]. Also according to the same author, gliadin is considered the main toxic agent that causes the disease, which can be divided into four fractions: alpha, beta, gamma, and omega [30].

## Immune Factors

Celiac disease is an autoimmune disease, associated with a genetic predisposition and tTG. This enzyme can be considered responsible for the mediation of gliadin discouragement, where glutamic acid residues occur that have negatively charged epitopes that will effectively interconnect to the HLA allele and are then recognized by T cells. The immune system is directly affected by gliadin peptides, which are responsible for stimulating immunity. This may be innate or adaptive [31].

Some authors say that the intestinal epithelium is composed of enterocytes that interconnect from the intercellular junctions. Such junctions, when they occur in an individual in a healthy organism, work in a way that makes them waterproof, which prevents the passage of molecules through it. There is still no exact knowledge related to the passage of gliadin through the epithelium, but there are some hypotheses. One of these hypotheses is the belief that this passage occurs through the paracellular pathway, through the existence of a protein known as zonulin. There is also the hypothesis of passage through retro transcytosis from a membrane receptor [31].

## Gluten in Food

Botelho et al. (2007) explain that gluten is a substance that has an elastic consistency, being insoluble in water and adherent, thus becoming responsible for the structure of most food. It consists of gliadin and glutenin. Its formation occurs from the hydration of these proteins linked together with other macromolecular components. Such a process takes place through several types of chemical bonds. The only cereal that contains glutenin and gliadin in an amount necessary to form gluten is wheat. However, there may also be the presence of these proteins in cereals such as oats, rye, and barley, in the form of avenin, secalin, and hordein. Glutenin and gliadin serve as the basis for the use of wheat flour when preparing pasta and bakery products. This is due to the functionality of these proteins in question, where they are determinants at the time of food acceptance, which can directly affect the sensory quality. The properties can intervene in the development of sensory, structural, kinesthetic characteristics, etc. [22].

Gliadins are considered single-chain proteins, having a sticky and gummy characteristic, being responsible for the consistency and viscosity of the dough. Glutenins, on the other hand, have a branched-

chain, being elastic, but not cohesive. Having a fundamental role in the extensibility of the mass. Something very necessary when it comes to pasta and bakery foods. The polypeptide fragments that are responsible for making up the gluten fraction are known as prolamines. This being completely toxic to patients with CD [1,2].

Still, gluten is a protein of paramount importance for the food processes that need growth, considering that thin membranes are formed that hold the produced gas bubbles that are produced by the growth agents. When gluten comes in contact with heat, it becomes denatured. Creating a crust and limiting the orifices that are produced from the expense of gas inside the dough, providing a crunchy aspect to the products created [22].

Also, gluten-containing cereals can be used during food preparation or processing. Commonly, it is found in industrialized products, such as powdered coffee, chocolate, sauces, chewing gum, among others. Gliadin may even be present in something due to contamination of wheat flour in the environment, in utensils, or even in food handlers who work in the preparation of products. There is a need to take extreme care at the time of cleaning so that nothing is contaminated [15].

## Food Practices

Beyer (2002) informs that in the western diet the feeding is based in the majority of the cases based on wheat [26]. This makes it very difficult for people with celiac disease to follow a zero-gluten diet to the letter. Demanding then that these have a deep determination. And, in addition, celiac disease can interfere even in the social life of its sufferer, because, in moments such as trips, meetings with friends/family, food outside the home, they can become a big problem [32,33].

## Conclusion

From the construction of the work that was presented, it became clear that it is of the utmost importance that celiac disease is diagnosed as soon as possible, otherwise, many problems can be caused in the body. In addition, it is necessary to offer as much information as possible, so that those who have the disease have an understanding of their limitations and the reason for them, then following the only treatment, food reeducation where foods containing gluten cannot be eaten. The more information you get to the carrier,

the more it can adapt to your needs, thereby reducing your risks and symptoms. As a result, industries are aware of their responsibility when it comes to producing and creating products. For it is necessary that everyone, without exception, has access to healthy and quality food.

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**Informed consent**

Informed written consent obtained from the participant

**Conflict of interest**

The authors declare no conflict of interest.

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