



## Genetic markers of non-celiac gluten sensitivity

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**Geovana Caetano Lobo**  
**Isadora Vilela Aguiar**

### 1 INTRODUCTION

Non-celiac gluten sensitivity is a functional disorder, occurring in individuals in whom celiac disease and wheat allergy have been ruled out. It is characterized by intestinal symptoms such as abdominal pain, bloating, diarrhea, epigastric pain, nausea, and constipation; extraintestinal symptoms such as headaches, musculoskeletal and skin manifestations, chronic fatigue, and difficulty concentrating may also occur. They occur hours to days after the ingestion of gluten-containing foods, and disappear after its removal from the diet. There are still no specific tests that can diagnose it, and the diagnosis is made by exclusion. Although non-celiac gluten sensitivity has a high prevalence, its diagnosis and pathophysiology are still highly questioned, and it is certainly a subject worthy of further, well-conducted studies. In view of the above, the following guiding problem emerged in this research: what are the genetic markers of non-celiac gluten sensitivity?

### 2 OBJECTIVE

To understand the functioning of the organism of patients with non-celiac sensitivity to gluten and its genetic markers, which is a pathology that is little talked about, but quite present in society. The evidence was based on studies and scientific papers already published, in order to conclude the validity or otherwise of the working hypotheses established

### 3 METHODOLOGY

This research refers to a bibliographic survey, in which scientific papers and articles published in The Lancet; Scielo; Published online; Brazilian Journal of health Review will be used as a source of research. The selected theses will go through a selection, so that they are of great relevance for this analysis. The most recent and current ones will be selected. Active reading and study of the chosen references will be carried out so that a positive and relevant result can be reached from the selection of the best information, having chosen the paths to be followed.



## 4 DEVELOPMENT

Non-celiac gluten sensitivity (NCGS) is defined as adverse reactions to gluten when celiac disease and wheat allergy have been ruled out, since individuals with NCGS may experience similar symptoms as people with celiac disease, but they test negative for IgA biomarkers and intestinal damage associated with celiac disease. Although SGNC has had case descriptions since 1980, it still does not have well-established epidemiology, pathophysiology, clinical spectrum, and treatment of SGNC (CATASSI et al., 2015). The prevalence in the general population is unknown, but it has been estimated to be between 0.5 and 6% in different countries, which is estimated to be six to ten times higher than that of celiac disease (RESENDE; SILVA; MATTOS SCHETTINO; LIU, 2017).

Research has shown that the human leukocyte antigen (HLA) gene is the most important genetic predictor of gluten intolerance. HLA genes produce a group of proteins called the human leukocyte antigen complex that are responsible for differentiating proteins in the body and foreign bodies. Over 99% of people with celiac disease and 60% of those with SGNC have the risk version DQ2 or DQ8 of HLA. Genetic screening is important since about 70% of the population does not have the HLA-DQ2 and DQ8 risk genotypes. Thus most people do not need to undergo serological testing and invasive biopsy for celiac disease. Therefore they should be reserved for individuals who have HLA-DQ2 or DQ8 risk genotypes. A positive genetic test result for HLA-DQ2 or DQ8 is not a diagnosis of celiac disease; but having a negative result for HLA-DQ2 and DsQ8 indicates that celiac disease can be ruled out.

Unlike CD, in which there is activation of the adaptive immune response, in CNMS there is only an innate immune response against the harmful agent. This response, which does not require HLA-DQ2/DQ8, can cause increased intestinal permeability, followed by a low-intensity inflammatory response in the intestinal mucosa, with release of cytokines and gastrointestinal peptides. The involvement of the enteric cholinergic nervous system by these mediators would eventually favor the onset of digestive symptoms such as abdominal pain, flatulence, dyspepsia, or diarrhea

Treatment of non-celiac gluten sensitivity is by diet, through the withdrawal of gluten-containing foods. The improvement of symptoms with this withdrawal does not confirm the diagnosis of the disease, since it may be due to the fact that gluten and FODMAPs (fermentable Oligosaccharides, Disaccharides, Monosaccharides, and Polyols) are foods metabolized by the microbiota with gas production, which, added to the osmotic action, leads to distension, pain, and flatulence. Moreover, there is a semiological similarity between the manifestations of CNMS, celiac disease, and irritable bowel syndrome, and since the removal of gluten from the diet is also beneficial for these conditions, it is challenging to distinguish between them, and there may even be an overlap between them, as shown in a population-based study in Northern Europe in which IBS was found in between 16 and



25% of the people, and in a subsample of these, a double-blind, placebo-controlled gluten challenge was carried out, confirming SNCG in 28% of the cases.

## **5 CONCLUDING REMARKS**

Although the understanding of the functioning of the SNCG has a significant number of researchers, its diagnosis and pathophysiology are still highly questioned. Thus, the use, with or without medical recommendation, of a gluten-free diet becomes a common practice, with possible harmful effects on the nutritional status of those involved. Thus, the development of more elaborate studies on genetic markers of non-celiac gluten sensitivity is important, since it is a disease with high prevalence and popular repercussions. Through this knowledge, it will facilitate research and the search for appropriate treatments.



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