

Nutritional status variation and intestinal and extra intestinal symptomatology in patients with celiac disease and non-celiac gluten sensitivity given specialized dietary advice

*Evolução do estado nutricional e sintomatologia intestinal e extra intestinal em pacientes com doença celíaca e sensibilidade ao glúten não celíaca submetidos à orientação dietética especializada*

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## ABSTRACT

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### Objective

To investigate the nutritional status variation and symptomatology of patients with celiac disease and non-celiac gluten sensitivity after specialized dietary advice.

### Methods

This prospective study included 80 patients with celiac disease and non-celiac gluten sensitivity. Clinical, metabolic, and nutritional variables were collected from medical records, and the symptomatology was investigated by the

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Metabolic Screening Questionnaire. The variables were assessed on two occasions (T1 – before dietary advice and T2 – after dietary advice) with an interval of three months between T1 and T2.

### Results

The median age was 42 years. The prevalences of celiac disease and non-celiac gluten sensitivity were 66.2% and 33.8%, respectively. Normal weight prevailed at T1 (58.8%) and T2 (56.3%), but 30.0% of the patients at T1 and 34.9% of the patients at T2 had excess weight. The two conditions had similar symptomatology. The most frequent signs and symptoms on both occasions involved the gastrointestinal tract, followed by energy/activity and emotions. All symptoms decreased significantly after the introduction of a proper diet.

### Conclusion

The patients were normal weight on both study occasions (T1 and T2), and the symptoms improved after dietary advice. Thus, we reinforce the importance of proper dietary management in both clinical conditions to make dietary adjustments that improve these individuals' symptomatology.

**Keywords:** Celiac disease. Diet. Food and nutrition education. Non-celiac gluten sensitivity. Signals and symptoms.

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## RESUMO

### Objetivo

*Investigar a evolução do estado nutricional e a sintomatologia de pacientes com doença celíaca e sensibilidade ao glúten não celíaca após orientação dietética especializada.*

### Métodos

*O estudo prospectivo foi realizado com 80 pacientes portadores da doença celíaca e de sensibilidade ao glúten não celíaca. A coleta das variáveis clínicas, metabólicas e nutricionais foi feita por análise dos prontuários, enquanto a sintomatologia foi investigada por meio de Questionário de Rastreamento Metabólico. As variáveis foram avaliadas em dois momentos (T1 – antes da orientação dietética e T2 – após orientação dietética), com intervalo de 3 meses entre T1 e T2.*

### Resultados

*A mediana de idade foi de 42 anos. A prevalência de doença celíaca e de sensibilidade ao glúten não celíaca foi de 66,2% e 33,8%, respectivamente. A eutrofia prevaleceu como estado nutricional de T1 (58,8%) e T2 (56,3%), porém 30,0% dos pacientes em T1 e 34,9% em T2 apresentaram excesso de peso. A sintomatologia foi similar entre as duas enfermidades. Os sinais e sintomas mais frequentes nos dois tempos foram os do trato digestório, seguido pelos relacionados à energia/atividade e às emoções. Todos os sintomas diminuíram significativamente após a introdução da dieta.*

### Conclusão

*Os pacientes apresentaram estado nutricional de eutrofia nos dois momentos avaliados (T1 e T2) e houve redução dos sintomas após as orientações nutricionais. Dessa forma, reitera-se a importância do manejo dietético adequado para ambas as enfermidades clínicas a fim de adequar a dieta que favoreça a melhora da sintomatologia apresentada por esses indivíduos.*

**Palavras-chave:** Doença celíaca. Dieta. Educação alimentar e nutricional. Sensibilidade não celíaca ao glúten. Sinais e sintomas.

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## INTRODUCTION

Celiac disease is a chronic inflammatory intestinal disease characterized by permanent intolerance to gluten, the main protein fraction of wheat, rye, barley, and oats<sup>1</sup>. This condition is mediated by T lymphocytes in genetically

susceptible individuals and may cause lesions in the intestinal mucosa and reduce nutrient absorption<sup>1-3</sup>. Many years ago, celiac disease was considered a pediatric disease, but currently, adults have been increasingly diagnosed with the condition, demonstrating that this disease may affect people of any age<sup>4</sup>.

From the 1980s onward, celiac disease was no longer considered a rare disease, and today, it affects 0.5 to 1.0% of the global population, with important regional variations<sup>5</sup>. In Western countries celiac disease affects approximately 1.00% of the general population<sup>6</sup>. In Brazil official statistics on celiac disease epidemiology are unknown, but new studies show that celiac disease is found in 0.15 to 1.75% of the general population<sup>7</sup>. Additionally, first-degree relatives of celiacs share genetic and environmental risk factors for celiac disease and consequently, are 10 to 20 times more likely to develop the disease than the general population<sup>7</sup>.

Non-Celiac Gluten Sensitivity (NCGS) was originally described in the 1980s and has been 'rediscovered' recently. It is characterized by intestinal and extra-intestinal symptoms related to the intake of gluten-containing foods by individuals who do not have celiac disease or wheat allergy<sup>8</sup>. NCGS epidemiology is still unknown and far from being established especially because many patients currently self-diagnose and begin a gluten-free diet without medical and nutritional advice, and disease-specific biomarkers are not available<sup>8,9</sup>.

In Non-celiac gluten sensitivity adverse reactions to gluten are not followed by the emergence of autoantibodies and do not change the intestinal barrier. Immune system involvement is more limited, and this explains how this condition is not accompanied by autoimmune phenomena during reaction to gluten. NCGS symptoms may be similar to the gastrointestinal symptoms associated with celiac disease. Thus, a diagnosis of NCGS is usually done by exclusion<sup>9</sup>.

Celiac disease has three types of clinical manifestations: classical or typical, non-classical or atypical, and asymptomatic or silent. The first type, classical, is characterized by the presence of intense gastrointestinal symptoms, such as diarrhea, vomiting, and abdominal distention, among others. The second type, atypical, presents a set of extra-intestinal symptoms in which digestive symptoms are absent or, when present,

are secondary. The silent form has no clinical manifestations<sup>1,3</sup>.

Globally, both celiac disease and NCGS are considered public health problems because of the global distribution, prevalence, and probability of the development of severe complications<sup>10,11</sup>. Hence, along with the clinical manifestations, it is important to consider the patients' nutritional status as the proportion of celiacs with excess weight at diagnosis is increasing. Currently, the greatest concern regards patients that gain weight on a gluten-free diet secondary to better nutrient absorption<sup>12</sup>. Excess weight is associated with the risk of developing comorbidities, such as metabolic syndrome, diabetes *Mellitus* type 2, cardiovascular diseases, and some forms of cancer<sup>12</sup>.

Treatment is exclusively dietary and requires a gluten-free diet for patients with celiac disease and a low gluten diet for patients with NCGS<sup>13</sup>. The diet should be monitored by a dietitian and other health professionals as monitoring improves adherence and aims to reduce the risk of long-term complications<sup>2</sup>.

It is essential to assess the consequences of the dietary treatment on the nutritional status of patients with celiac disease and NCGS to reduce the negative impact of excess weight<sup>12,14,15</sup>. Therefore, this study aimed to investigate the intestinal and extra-intestinal signs and symptoms of celiac disease; to distinguish celiac disease and NCGS symptoms; and to verify whether dietary advice affects nutritional profile and symptomatology. The results provide additional information on individuals with celiac disease and NCGS, contributing to a better understanding of the changes in the symptomatology of both clinical conditions in response to dietary treatment.

## METHODS

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This is a prospective study of participants of a care program provided by a public university

from *Minas Gerais*, Brazil from January 2013 to July 2014 created specifically for individuals with intestinal disorders.

The study was approved by the Human Research Ethics Committee of the *Universidade Federal de Viçosa* (under Protocol nº 30424514.3.0000.5153). All participants were informed about the study objectives and signed an Informed Consent Form which guaranteed the study's compliance with the norms of Resolution 466 of the National Health Council. Moreover, all participants received dietary advice and were followed in the long term by outpatient appointments and social events (cooking workshops provided by the program) during adaptation to the new eating habits.

The sample consisted of 80 adults and older adults with celiac disease or NCGS. The participants were selected randomly, but to be included in the study, individuals had to have medical tests and/or referrals that confirmed celiac disease or NCGS diagnosis and had to have participated in the care program for patients with intestinal disorders for at least six months. Individuals aged less than 18 years and those without a diagnosis of celiac disease or NCGS were not included.

## Procedures

Anthropometric (body weight, height, and percentage of body fat determined by bioelectrical impedance analysis), social, clinical, and Metabolic Screening Questionnaire data were collected from the patients' medical records.

Body Mass Index (BMI) was calculated by dividing the weight by the square of the height ( $\text{kg}/\text{m}^2$ ). Adults' BMI were categorized as recommended by the World Health Organization<sup>16</sup> as follows:  $\text{BMI} < 18.5 \text{kg}/\text{m}^2$  as underweight;  $18.5 \leq \text{BMI} \leq 24.9 \text{kg}/\text{m}^2$  as normal weight;  $25 \leq \text{BMI} \leq 29.9 \text{kg}/\text{m}^2$  as overweight, and  $\text{BMI} \geq 30 \text{kg}/\text{m}^2$  as obese. Older adults' BMI were categorized as recommended by Lipschitz<sup>17</sup> as

follows:  $\text{BMI} < 22 \text{kg}/\text{m}^2$  as underweight;  $22 \leq \text{BMI} \leq 27 \text{kg}/\text{m}^2$  as normal weight, and  $\text{BMI} > 27 \text{kg}/\text{m}^2$  as overweight.

Individuals diagnosed with celiac disease received advice on a gluten-free diet, and those with NCGS received advice on a low-gluten diet<sup>13</sup>. In addition to the dietary plans, the participants received individual nutritional support. The Metabolic Screening Questionnaire identified the manifested signs and symptoms<sup>18</sup>. This instrument consists of 14 blocks on the body's functional aspects and behavioral activities. The interviewee answered the questions presented in the form of an interview. The answers were scored 0 to 4 based on the level of symptom intensity, where 0 indicated the absence of symptoms; 1, occasional non-severe symptom; 2, occasional severe symptom; 3, frequent non-severe symptom; and 4, frequent severe symptom. The metabolic, clinical, and anthropometric variables were assessed on two occasions (T1 – before dietary advice and T2 – after dietary advice) during the individual appointments, with an interval of three months between T1 and T2.

The sample was characterized by distribution of frequencies and estimates of measures of central tendency and dispersion. The Kolmogorov-Smirnov test investigated whether the data had normal distribution, the Wilcoxon's *t*-test verified the difference between nutritional status and symptoms at T1 and T2, the Student's *t*-test compared the mean percentages of body fat at T1 and T2, and the Mann-Whitney U-test verified the difference between celiac disease and NCGS symptoms. The study used a significance level of  $\alpha < 5\%$ . The data were processed and analyzed by the software Statistical Package for the Social Sciences (SPSS Inc., Chicago, Illinois, United States of America) version 20.0.

## RESULTS

The sample consisted of 80 adults and older adults, of which 80.00% were females,

66.25% had celiac disease, and 33.75% had NCGS. The median age was 42 years, mean age, 41.24 years (Standard Deviation, SD=12.773), minimum age, 18 years, and maximum age, 65 years. Table 1 describes the patients' social and health characteristics.

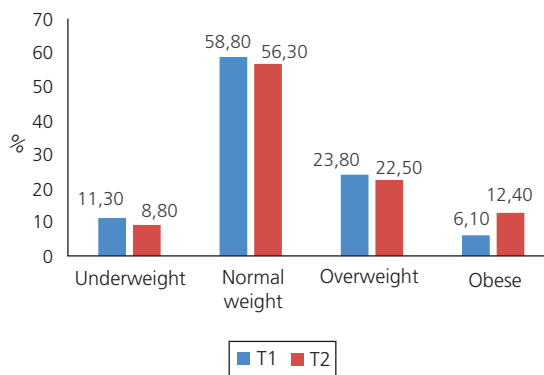
The most prevalent nutritional status at T1 and T2 was normal weight, but 30.0% of the

patients at T1 and 34.9% of the patients at T2 had excess weight (Figure 1). The BMI of patients with celiac disease or NCGS did not differ significantly between T1 and T2 according to the Wilcoxon's *t*-test (Table 2). Likewise, the percentages of body fat determined by bioelectrical impedance analysis did not differ between T1 and T2 according to the Student's *t*-test (Table 2).

The means for the signs and symptoms presented by patients with the two conditions at T1 and T2 differed significantly for all organs, physical structures, and behavioral activities (Table 3).

**Table 1.** Frequencies of the social and health characteristics of patients with celiac disease and non-celiac gluten sensitivity. Viçosa (MG), Brazil, 2014.

Variables	n	%
<i>Age (years)</i>		
Adults (18-60 years old)	75	93.8
Older adults (60 years old or older)	5	6.2
<i>Gender</i>		
Male	16	20.0
Female	64	80.0
<i>Smoker</i>		
Yes	7	8.8
No	60	75.0
Ex-smoker	13	16.2
<i>Consumes alcoholic beverages</i>		
Yes	35	43.8
No	39	48.8
Used to consume	6	7.4
<i>Physically active</i>		
Yes	42	52.5
No	38	47.5



**Figure 1.** Nutritional status of patients at the first (T1) and last (T2) appointments according to body mass index. Viçosa (MG), Brazil, 2014.

**Table 2.** Anthropometric profile of patients with Celiac Disease (CD) and Non-Celiac Gluten Sensitivity (NCGS) at the first appointment (T1) and last appointment (T2). Viçosa (MG), Brazil, 2014.

Variables	Total (n=80)			<i>p</i>	CD (n=53)			<i>p</i>	NCGS (n=27)			<i>p</i>
	M	±	SD		M	±	SD		M	±	SD	
Age (years)	41.24	±	12.77		40.53	±	12.08		42.63	±	14.17	
Weight (kg)				0.427*				0.191*				0.440*
T1	63.07	±	14.90		62.09	±	15.19		64.98	±	14.41	
T2	63.81	±	15.24		63.19	±	15.29		65.11	±	15.37	
BMI (kg/m <sup>2</sup> )				0.451*				0.214*				0.530*
T1	23.80	±	5.09		23.59	±	4.94		24.20	±	5.46	
T2	24.08	±	5.26		23.96	±	5.00		24.33	±	5.85	
%BF				0.186 <sup>B</sup>				0.284 <sup>B</sup>				0.451 <sup>B</sup>
T1	24.73	±	7.53		24.39	±	7.84		25.42	±	6.95	
T2	25.57	±	8.65		24.99	±	8.88		26.90	±	8.14	

Note: \*Wilcoxon's *t*-test; <sup>B</sup>Paired Student's *t*-test.; T1: First Appointment; T2: Last Appointment.

BMI: Body Mass Index; BF: Body Fat, M: Mean; SD: Standard Deviation.

At T1, the most prevalent symptoms were intestinal (diarrhea, nausea, vomiting, constipation, distended/swollen abdomen, eructation, flatulence, heartburn, and stomach/intestinal cramping), followed by extra-intestinal symptoms related to energy/activity (fatigue, enervation, hyperactivity, and difficulty resting) and emotions

(mood changes, anxiety, fear, irritability, aggressiveness, and depression).

At T2, after the dietary intervention, the most prevalent symptoms again were intestinal, followed by emotions and mental activities (poor memory, confusion, poor concentration, poor motor coordination, learning difficulties, and

**Table 3.** Means of the most prevalent signs and symptoms in patients with celiac disease and non-celiac gluten sensitivity before and after dietary advice. Viçosa (MG), Brazil, 2014.

Variables	T1			T2			<i>p</i> *
	M	±	SD	M	±	SD	
Head	6.30	±	4.14	1.53	±	2.57	<0.001
Eyes	5.54	±	4.01	1.46	±	2.69	<0.001
Ears	3.40	±	3.62	0.78	±	1.80	<0.001
Nose	6.19	±	5.94	1.56	±	3.39	<0.001
Mouth/throat	5.83	±	5.05	1.23	±	2.47	<0.001
Skin	8.03	±	5.82	2.90	±	3.69	<0.001
Gastrointestinal tract	17.81	±	6.28	6.03	±	5.35	<0.001
Joints/muscles	6.51	±	5.57	1.75	±	3.57	<0.001
Energy/activity	10.29	±	5.38	2.80	±	4.01	<0.001
Mind	9.01	±	7.36	3.63	±	5.65	<0.001
Emotions	9.56	±	4.88	3.66	±	4.29	<0.001
Heart	3.09	±	3.75	0.60	±	1.85	<0.001
Lungs	3.34	±	4.19	0.76	±	2.37	<0.001
Other	8.09	±	7.67	1.82	±	3.15	<0.001

Note: \*Statistically significant. Wilcoxon's *t*-test.

T1: First Appointment; T2: Last Appointment; M: Mean; SD: Standard Deviation.

**Table 4.** Means of the signs and symptoms presented by patients with celiac disease and Non-Celiac Gluten Sensitivity (NCGS) at the first appointment (T1). Viçosa (MG), Brazil, 2014.

Variables	Celiac disease			NCGS			<i>p</i>
	M	±	SD	M	±	SD	
Head	6.00	±	4.38	6.62	±	3.86	0.291
Eyes	5.32	±	4.13	5.96	±	3.80	0.429
Ears	3.15	±	3.70	3.88	±	3.47	0.258
Nose	7.05	±	6.61	4.48	±	3.93	0.189
Mouth/throat	6.07	±	4.99	5.33	±	5.24	0.456
Skin	7.39	±	5.48	9.25	±	6.35	0.230
Gastrointestinal tract	17.96	±	7.14	17.51	±	4.23	0.491
Joints/muscles	6.26	±	4.97	7.00	±	6.66	0.967
Energy/activity	9.96	±	5.57	10.92	±	5.00	0.346
Mind	8.67	±	7.53	9.66	±	7.12	0.441
Emotions	9.15	±	4.82	10.37	±	4.97	0.229
Heart	2.45	±	3.78	4.33	±	3.43	0.007*
Lungs	3.13	±	4.15	3.74	±	4.32	0.464
Other	8.30	±	8.17	7.66	±	6.70	0.838

Note: \*Statistically significant. Mann-Whitney U-test.

M: Mean; SD: Standard Deviation.

decision-making difficulties). However, all symptoms presented by patients with celiac disease and NCGS improved significantly after the introduction of gluten-free and low-gluten diets, respectively.

Comparison of the means of the signs and symptoms of patients with celiac disease and NCGS found no difference between the groups. The only variable that differed significantly regarded cardiac signs and symptoms (Table 4).

Comparison of the means of the variables of organs and physical structures (head, eyes, ears, skin, joints, heart, and lungs) and behavioral activities (energy, mental activities, emotions) showed that individuals with NCGS had higher means than celiacs, but the difference was not significant. On the other hand, the means of the other variables (nose, mouth, gastrointestinal tract, and others, such as genital itching or discharge, miscarriage, loss of appetite, and anemia) were higher in celiacs.

## DISCUSSION

The median age of the 80 adults and older adults who constituted the sample was 42 years, and 80% were women. Volta & De Giorgio<sup>9</sup> corroborate the present findings; although NCGS occurs at any age, it seems to be more frequent in adults with a median age of 40 years (ranging from 17 to 63 years), and more prevalent in females than males<sup>9</sup>.

Other studies support the present study findings. Reilly & Green<sup>6</sup> also affirmed that the highest prevalences of celiac disease have occurred in adult females, and that celiac disease has mostly been diagnosed in later life<sup>6</sup>. In addition Araújo<sup>19</sup> and Polanco<sup>20</sup> found that celiac disease is more common in women, and the latter reported that celiac disease affects women in a ratio of 2 to 1<sup>19,20</sup>.

Most patients with celiac disease and NCGS had normal weight at T1 and T2.

Nevertheless, 30.0% of the patients at T1 and 34.9% of the patients at T2 had excess weight. These data are similar to those reported by Ukkola *et al.*<sup>12</sup>, who found that 57.0% and 39.0% of their 698 celiacs had normal weight and excess weight, respectively, at the beginning of their study. After being on a gluten-free diet for one year, 54.0% and 45.0% of the sample had normal weight and excess weight, respectively<sup>12</sup>.

Recent population-based studies have found an increasing mean BMI in Western countries, and today, about half the adult population is overweight or obese. This trend was similar to the trend observed in the present sample of patients with celiac disease and NCGS as 34.9% of the patients had excess weight in the last appointment<sup>12</sup>.

Araújo<sup>19</sup> found that malnutrition and excess weight were the most common nutritional statuses in celiacs. Malnutrition stems from the difficulty of consuming food because of the problems and poor nutrient absorption caused by impaired intestinal mucosa permeability. On the other hand, excess weight stems from better nutrient absorption due to improvements in the absorptive structure of the intestinal membranes and symptoms, stimulating higher food intake. Moreover, foods for celiacs usually have higher lipid contents, increasing the weight of celiacs in treatment.

Individuals with celiac disease and NCGS complain that the availability of sensorially pleasant foods is small and that the products available in grocery stores are usually very expensive<sup>11,21</sup>. The lack of cooking skills and time to prepare gluten-free foods add to the difficulty of consuming unusual foods<sup>22</sup>.

An effective treatment for all clinical forms of celiac disease is essentially dietary, requiring the removal of gluten from the diet or its reduction in the case of NCGS<sup>13</sup>. Thus, it is important to reinforce the need of dietary monitoring by a dietitian<sup>19</sup>.

Given the difficulty of removing or reducing gluten-containing grains from one's diet,

dietitians' conduct, from assessment and control of nutritional status and during treatment, should aim to eliminate the signs and symptoms of patients with celiac disease and NCGS. Hence, to ensure proper nutritional status and good quality of life, said conduct should empower the patient to choose and prepare foods, to avoid cross-contamination during food preparation and distribution, and to be aware of metabolic conditions, such as impaired absorption.

The study results corroborate Casemiro<sup>22</sup> as most of his patients were normal weight and a small percentage was underweight after the introduction of a gluten-free diet<sup>22</sup>. This finding may also stem from patient participation in the program developed for individuals with intestinal disorders. The program includes individual care and group advice during cooking workshops. In addition to receiving nutritional advice during treatment, the patients also receive recipes of healthy gluten-free preparations high in vitamins, minerals, and fibers. The patients are also invited to participate in social activities (cooking workshops), where they learn to make gluten-free preparations, interact with other patients, and share their anguishes, doubts, and achievements during treatment.

In the present study, 66.25% and 33.75% of the patients had celiac disease and NCGS, respectively, contrary to Volta & De Giorgio<sup>9</sup>, who believe that the presumed prevalence of NCGS is higher than that of celiac disease, even though NCGS epidemiology is far from being established. Nonetheless, one must consider the context of the study patients as they participate in a program designed for individuals with intestinal disorders.

The most evident symptoms in the Metabolic Screening Questionnaire were similar to those reported by Casemiro<sup>22</sup> as both studies found a prevalence of high irritability, abdominal bloating, abdominal pain, flatulence, and joint pain.

Whitacker *et al.*<sup>23</sup> investigated symptoms suggestive of celiac disease in diabetic children from *Campinas* (SP) and found that, of 195

children, 62 were asymptomatic, 91 had at least one gastrointestinal tract symptom, and 15 reported at least one unspecific symptom. In the present study, abdominal pain was the main complaint among classical symptoms, followed by abdominal distention, constipation, and epigastralgia. Frequent bouts of diarrhea, flatulence, and vomiting were also reported. In the same study, arthralgia was the most cited unspecific symptom, followed by fatigue<sup>23</sup>.

Ukkola *et al.*<sup>12</sup> found the classical form of celiac disease in 70.0% of the patients, 9.0% presented extra-intestinal symptoms, and the remainder was asymptomatic<sup>12</sup>. Sdepanian *et al.*<sup>24</sup> also found the classical form of celiac disease in 88.9% of the patients, and 11.1% had the non-classical form. Of the 32 patients with non-classical manifestations, three presented only one symptom, two were underweight, and one was anemic<sup>24</sup>.

The present study results differ from those reported by Reilly & Green<sup>6</sup> and Ukkola *et al.*<sup>12</sup>, who found that the clinical picture of celiac disease has changed both in children and adults as diarrhea and malabsorption are increasingly uncommon (classical gastrointestinal symptoms). Currently, abdominal cramps and delayed growth are the main manifestations in children. The main manifestations in adults have been<sup>6</sup> anemia, osteoporosis, dermatitis herpetiformis, chronic fatigue, and varied neurological manifestations (extra-intestinal symptoms)<sup>12</sup>.

Celiac disease is an autoimmune disease that may affect any organ and not only the gastrointestinal tract, as once believed. Its outbreak and first symptoms may appear at any age. Additionally, the range of possible symptoms varies considerably between individuals, and even in the same individual during different phases of the disease<sup>25</sup>.

The present study found that all signs and symptoms presented by celiac disease and NCGS patients improved after adoption of a gluten-free and low-gluten diet, respectively. Said improvement suggests adherence to the gluten-



free or low-gluten diet as nonadherence would lead to symptom recurrence and persistence of the histological and serological changes. This finding is corroborated by Pratesi & Gandolfi<sup>25</sup>, who found that many patients experienced an undefinable general malaise before diagnosis, which improved after adherence to a gluten-free diet<sup>25</sup>. Likewise, Czaja-Bulsa<sup>26</sup> supports our data as they affirmed that a gluten-free diet leads to full symptom regression in patients with Non-celiac Gluten Sensitivity<sup>26</sup>.

According to Kotze<sup>27</sup>, adherence to a gluten-free diet makes symptoms, such as micro- and macronutrient malabsorption, diarrhea, and edema, disappear, whetting the appetite and improving nutritional status in a few days or weeks. Still, total or partial recovery of the intestinal mucosa functionality and histology may take 6 to 19 months, or in some cases, 24 to 48 months<sup>22,27</sup>.

The means of celiac disease and NCGS symptoms did not differ significantly. In this sense, Sapone *et al.*<sup>28</sup> affirmed that NCGS symptoms may resemble those of celiac disease, but NCGS has a higher prevalence of extra-intestinal symptoms, such as behavioral changes, bone or joint pain, cricks, weight loss, and chronic fatigue<sup>28</sup>.

Between 2004 and 2010, 5,896 patients were followed by the University of Maryland Center for Celiac Research<sup>28</sup>. The symptoms found in patients with NCGS include: abdominal pain (68%); eczema and/or itching (40%); headache (35%); brain fog (34%); fatigue (33%); diarrhea (33%); depression (22%); anemia (20%); numbness in the legs, arms, or fingers (20%); and joint pain (11%)<sup>28</sup>.

Individuals with NCGS do not tolerate gluten and may develop gastrointestinal symptoms similar to those of celiac disease, although the clinical picture usually is less severe. The present study and Sapone *et al.*<sup>29</sup> found that the most reported symptoms by both groups involved the gastrointestinal tract, followed by symptomatology associated with energy/activity and emotions.

The typical NCGS presentation is a combination of systemic symptoms and manifestations, such as head ache, muscle pain, muscle contractions, arm numbness, chronic fatigue, brain fog, loss of body mass, and anemia, or they may include behavioral disorders, such as depression<sup>26</sup>.

The diagnosis of NCGS is established when gluten allergy and celiac disease (auto-immune) are discarded, that is, the condition is diagnosed by exclusion of other conditions<sup>28</sup>. NCGS condition has also been associated with unexplained psychiatric and neurological diseases, such as cerebellar ataxia, peripheral neuropathy, schizophrenia, or autism, as well as other autoimmune diseases (lupus, psoriasis, and fibromyalgia, among others). Since symptoms in these patients may improve with a gluten-free diet, this may suggest nutritional sensitivity to gluten<sup>30</sup>.

## CONCLUSION

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Finally, celiac disease and NCGS cannot be distinguished clinically, since both conditions have similar symptoms. Therefore, given the aforementioned information, this study provided some pieces of evidence regarding changes in nutritional status, and in the intestinal and extra-intestinal symptomatology of patients with celiac disease and NCGS submitted to specialized dietary advice. However, this subject has been little explored, especially with regard to NCGS, and there is a long road ahead.

## CONTRIBUTORS

PVM RIBEIRO was the main author of the article, responsible for data collection and analysis, and article drafting. AP SANTOS was responsible for article drafting and writing. CS ANDREOLI and SMR RIBEIRO was responsible for article drafting and writing. MP JORGE was responsible for data analysis, and article drafting and writing. AVB MOREIRA supervised the study and was responsible for data analysis and article drafting.

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