

# Quality of Life and Nutritional Parameters of Celiac Patients in Mar Del Plata, Argentina

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## Research Article

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## Abstract

Background: Celiac disease (CD) is one of the most common causes of chronic malabsorption. The changes that occur in the diet due to the influence of gluten free diet (GFD) lead to a lower content in the intake of fiber and vitamins. Some authors point out that the higher cost of GF foods, the lower availability of those in social events, the impaired patient's quality of life, could influence the degree of adherence to the GFD. Our aims were to evaluate the nutritional status, identifying the factors that are associated with adherence to the gluten-free diet (DLG) and the quality of life of a group of CD patients in Mar del Plata. Methods: CD patients were recruited from outpatient of clinic and gastroenterology unit of Oscar Alende Hospital, Mar del Plata and Argentina Celiac Association and had blood drawn for micronutrients concentration. Quality of life was evaluated by SF12 questionnaire, factors and adherence to GFD were determined by factors questionnaire and the Celiac Dietary Adherence Test (CDAT). Results: 47% of the participants had high adherence to GFD. The large supply of gluten-free foods without options during social events was significantly associated with the worst adherence to GFD. The average concentrations of folic acid, magnesium, iron and vitamin B12 were within the normal ranges; however, 6.7, 7.0 and 33.3% of the low adherent group showed low serum concentrations of iron, vitamin B12 and folate, respectively, while 7.7 and 53.8% of the high adherent exhibited low serum concentrations of iron and folate, respectively. Approximately 14.2% had anemia, only 7.1% had iron deficiency anemia. 54% of patients reported eating corn-based foods 3 or more times per week. The general perception of health was low in the age range between 18

and 40 years ( $34.3 \pm 22.0$ ) and the energy and vitality values were low in the same group ( $37.5 \pm 25.2$ ). Conclusions: Evaluation of quality of life and micronutrients indicate the need to support the patients in their treatment and to increase the supply of GF foods and the supplementation with vitamins and micronutrients of the GFD.

**Keywords:** Adherence; Celiac Disease; Gluten-Free Diet; Micronutrients; Quality of Life

**Abbreviations:** CD: Celiac Disease; GFD: Gluten Free Diet; HRQOL: Health Related Quality of Life; FQ: Factors Questionnaire; CDAT: Celiac Dietary Adherence Test; PCS: Physical Component Summary; PF: Physical Functioning; PR: Physical Role; GH: General Health; MCS: Mental Component Summary; SF: Social Functioning; E/V: Energy/Vitality; ER: Emotional Role; SM: Mental Health.

## Introduction

The gluten-free diet (GFD) is the only treatment indicated in celiac disease (CD) [1,2]. The GFD includes foods that naturally do not contain gluten and those foods that by their preparation are indicated as GF. Some studies report that GFD is associated with some nutritional deficiencies due to the exclusion of cereals that contain gluten and provide vitamins and minerals. The changes that occur due to the influence of a GFD lead to a lower content in the intake of fibers, vitamins and minerals with the consequent decrease in serum concentration of folate, iron, calcium, magnesium, vitamin B<sub>12</sub> and ferritin [3]. In our country, some studies reported nutritional deficiencies in celiac children under treatment but studies in adults are scarce [4].

Strict compliance to GFD may be affected by several factors. Some authors point out that the cost, the low availability of GF foods in social events and the low mood could influence the adherence to DLG [5]. Consequently, celiac patients may show different degrees of adherence to treatment. Food is an important part of a person's life, not only because it contributes to the well-being in their health but also because it collaborates in the style and quality of life. Previous studies on the impact of celiac disease and GFD on health-related quality of life (HRQOL) have yielded conflicting results, some research showed a decrease in HRQOL in celiac disease and other results estimated that it was comparable to that of the general population. Our aims were to evaluate the nutritional status of celiac people in Mar del Plata by determining the serum concentration of micronutrients, identify the factors that are associated with adherence to the gluten-

free diet (DLG) and evaluate the quality of life in that group of patients [6].

## Materials and Methods

Type of study: Descriptive, qualitative-quantitative, cross-sectional.

Sample: not probabilistic for convenience.

## Patients

Participants (age > 18 years) all had histologically confirmed CD, recruited from the Argentina Celiac Association (ACA) and the Gastroenterology Unit of Oscar Alende Hospital, Mar del Plata, Argentina, between October 2016 and September 2017. The diagnosis of celiac disease was made in all patients according to the criteria of the European Society of Pediatric Gastroenterology and Nutrition [7] and the Clinical Practice Guide on the Diagnosis and Treatment of celiac condition in the first level of care [1].

The patients were interviewed by a nutritionist or a qualified person, who used three questionnaires: Factors questionnaire (FQ), Celiac Dietary Adherence Test (CDAT) [8] and SF12 Questionnaire to evaluate Quality of Life [6].

The FQ was previously prepared by the working group and was applied in a former project (unpublished results) and was administered to assess the level of adherence and the aspects that influence the compliance to GFD.

The FQ included some items as symptoms, social and health team support, perception of adherence, general health status and difficulties in the compliance to diet, due to cost or accessibility to gluten-free foods in restaurants or social events. Adherence to GFD was assessed by the question that was included in the FQ: How often do you think you eat gluten (either voluntarily or involuntarily)? Adherence to the GFD was recorded on a scale ranging from high adherence: "Consume gluten less than three

times per year or once per year or once a month" to poor adherence "A GFD does not currently follow, consume gluten two or more times per month, once a week or several times per week" (Appendix 1. Factors 'questionnaire).

The high level of adherence was defined by the CDAT with a score of < 17. Additive CDAT score was calculated from 7 to 35 based on 7 questions each on a 5-point scale, with higher scores denoting worse GFD adherence.

### Quality of Life

SF-12 instrument consists of a subset of 12 selected elements of the SF-36 form that included the summary of the physical and mental domains which measure the presence and the severity of symptoms (abdominal pain, discomfort, diarrhea), others and their limitation on daily activities. The response options form Likert-type scales that assess intensity and frequency. The number of response options varies from three to six, depending on the element and each question receives a value that is subsequently transformed into a scale of 0 to 100. The scores have an average of 50 with a standard deviation of 10, so values greater than or less than 50, would indicate a good or worse status of health-related quality of life, respectively than the reference population. The physical component summary (PCS) included physical functioning (PF), physical role (PR), bodily pain (P) and general health (GH), while the mental component summary (MCS) included social functioning (SF), energy / vitality (E / V), emotional role (ER) and mental health (SM).

### Biochemical Analysis

Fasting venous blood samples were analyzed in the Central Laboratory of the Oscar Alende Hospital, Mar del Plata. Serum folate and serum vitamin B12 were analyzed by micro particles with enzyme immunoassay technology (MEIA) (AxSYM, Abbott, IL, USA); serum immunoglobulin A and ceruloplasmin were analyzed by an immunoturbidimetric method (ABBOTT 7000). Ferritin concentration was analyzed by chemiluminescent microparticle immunoassay (CMIA) (Architect Systems, Abbott). For the iron, magnesium, calcium and albumin concentration, a colorimetric method was used with a clinical chemistry analyzer (CB 400, Wiener Lab Argentina, manufactured in Italy).

Blood samples collected in K3 EDTA were analyzed in CELL-DYN Ruby counter (Abbott). The parameters reported were the concentration of red blood cells (RBC), mean corpuscular volume (MCV), hematocrit (Hct), hemoglobin concentration (Hb), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC) and white blood cells counts (WC), neutrophils, monocytes, lymphocytes, eosinophils and platelets.

The serum transglutaminase IgA (tTG IgA) was performed by an enzyme immunoassay (ELISA) with a recombinant human antigen (INOVA Quanta Lite human-tTG IgA, San Diego, USA; 97% sensitivity, 99% specificity).

### Statistical Analysis

A Student's t-test was used to assess the significant differences between the low and high adherence groups in serum micronutrient and macronutrients concentrations: calcium, albumin, iron, magnesium, vitamin B12 and folate, ceruloplasmin and ferritin.

For the analysis of the SF12 questionnaire, the results were analyzed with the Microsoft Excel program (97-2004), calculating measures of central tendency, dispersion. Internal consistency was analyzed using Cronbach's alpha coefficient, considering an alpha coefficient of 0.7 or more, as recommended in previous studies, acceptable for this study.

Differences between age groups and between sexes were calculated with the Student t-test with the IBM SPSS 22 software.

### Ethical Aspects

The protocol was approved by the Bioethics Committee of the Oscar Alende Hospital. Patients received complete information about the study and signed informed consent forms.

### Results

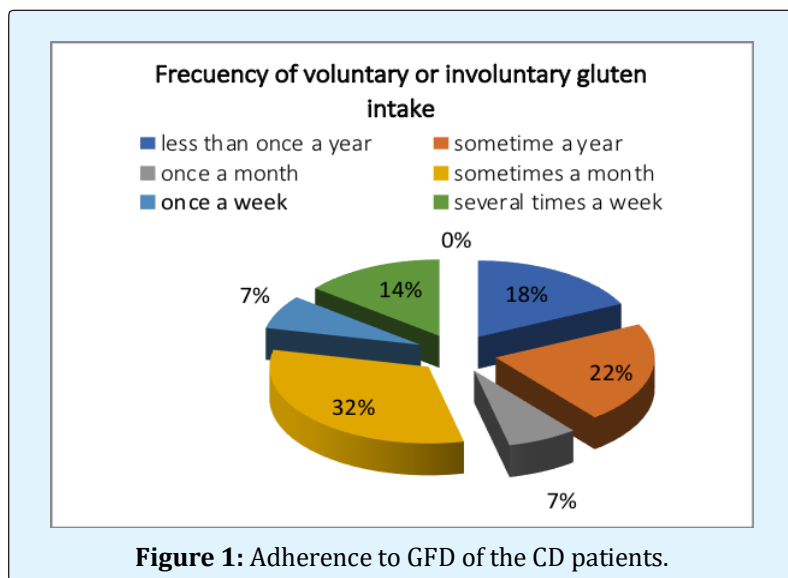
Twenty-eight patients participated; the mean age was 41 +/- 13 years (range 18 -72 years) and 24 (86 %) were female. The average age at diagnosis was 35 years (range 8-72 years) with the median time since diagnosis of 36 months (1-120 months) (Table 1).

	Total	High adherence	Low Adherence
Number of patients	28	13 (47 %)	15 (53%)
Age (years)	41	45	33
range	18-72	23-72	18-54
Gender			
Male	4	2	2
Female	24	11	13
Level of education *			
Low	7	4	3
Intermediate	19	8	11
High	2	1	1
Time since the diagnosis			
1-5 years	19	8	10
6-10 years	7	3	5
11-20 years	2	2	-
21-30 years	-	-	-
>30 years	-	-	-
Age at diagnosis			
<18 years	1	0	1
18-30	7	3	4
30-40	10	5	3
40-50	6	1	6
>50 years	4	4	1

**Table 1:** Characteristics of CD patients according with level of adherence to GFD. Data are presented as n (%) when appropriate.

The studied population adhered well to GFD, with almost 47 % being rated as high adherent by the FQ and 50% by the CDAT. Of the high adherence group, 7% didn't follow the diet once a month, 22% a few times a year and only 18% of the total surveyed no comply the diet once a

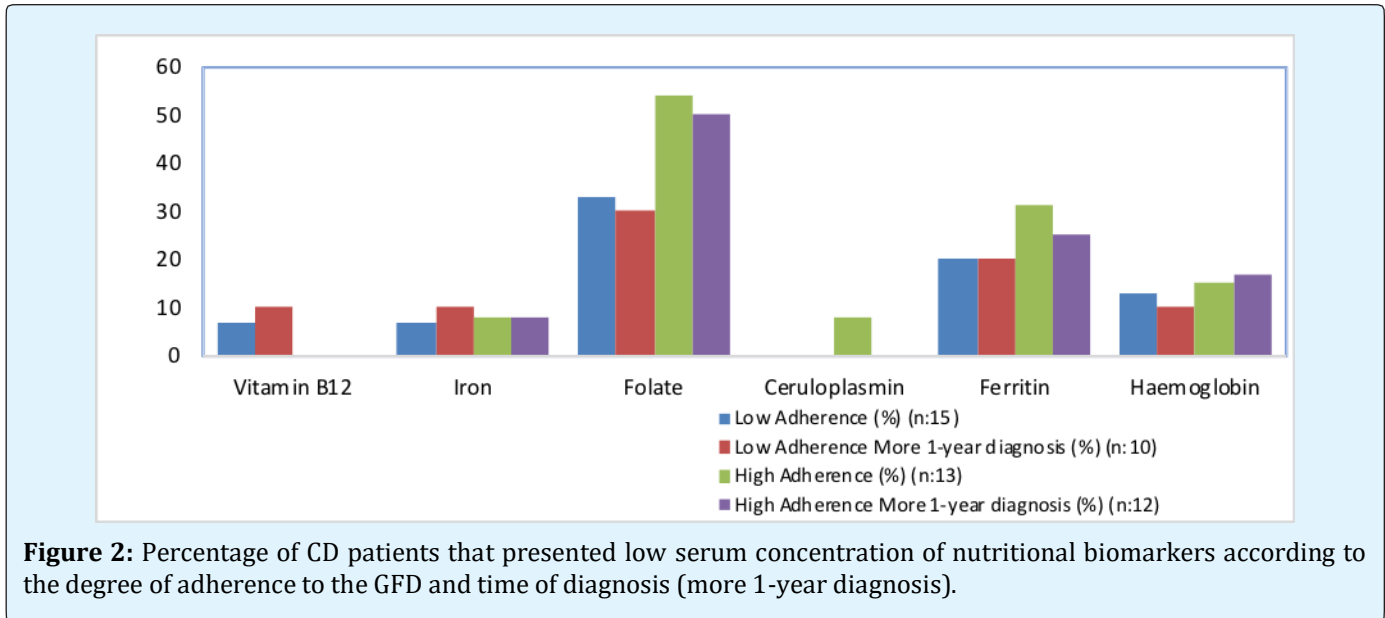
year. Of the low adherence group 32 % didn't follow the diet more than once a month, 7 % once a week and 14 % several times a week (Figure 1). Nearly 64.0 %, self-reported that they were adherent to the GFD.



Serum nutritional markers showed some deficiencies. Thus, 6.7% and 7.7% of patients with high and low adherence respectively had low serum iron concentration and only 7.0% of patients with low adherence had low serum vitamin B12 concentration.

46.4% of people with celiac disease showed a low serum folate concentration, with the most widespread

deficiency in those patients who reported high adherence (53.8%) compared to those with low adherence (33.3%). These results indicated that patients who follow a strict GFD have a higher prevalence of folate deficiency compared to those with low level of adherence to diet (Figure 2).



	High Adherence	Low Adherence	Significance differences #
Folate *			
Media and standard deviation	3.8 ± 2.8	4.6±4.17	Ns (p=0.3, p >0.05)
Range	1.0-10.4	1.6-18	
Magnesium *			
Media and standard deviation	2.0±0.21	2.0±0.16	Ns (p=0.5, p >0.05)
Range	1.74-2.42	1.76-2.33	
Iron *			
Media and standard deviation	110.5 ±32.41	117.6 ±38.35	Ns (p=0.3, p >0.05)
Range	44-139	54-194	
Vitamin B12 *			
Media and standard deviation	569.5 ±442.48	373 ±117.5	Ns (p=0.07, p >0.05)
Range	294 -greater 2000	173-549	

**Table 2:** Serum micronutrients concentration of patients with low and high adherence.

\*Reference interval (RI): Folate 3.1-20.5 ng/ml; magnesium 1.6-2.5 mg%; iron 65-180 ng/ml; vitamin B12 187-883 pg/ml).

# p values by Student's t-test.

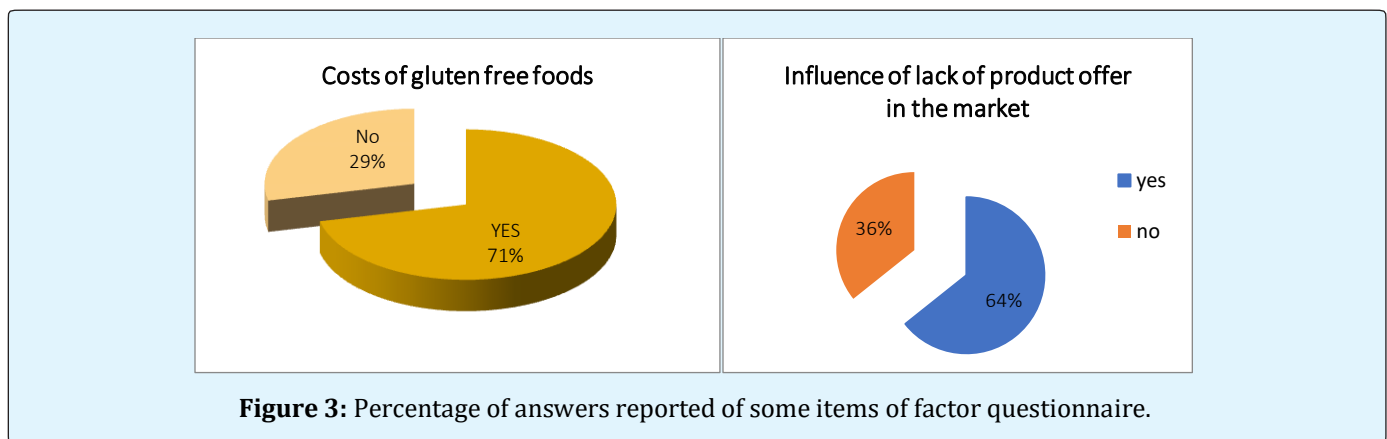
No significant differences were found in the mean serum concentration of folate, magnesium, iron and vitamin B12 between both groups, high and low adherence ( $p > 0.05$ ) (Table 2). The mean concentrations of folate, magnesium, iron and vitamin B12 were within the normal ranges for patients with high and low adherence.

No patient had low albumin levels and only 3.6% of CD patients had low serum ceruloplasmin levels.

The factor questionnaire did not show a significant association between the presence of symptoms and the level of adherence to the GFD ( $p=1,000$ ), 84% of patients responded that they had positive symptoms (abdominal pain, discomfort, diarrhea, others), but only 32% of the total said that these symptoms influenced the will to comply with the diet. Half of the population felt depressed and 64% of them said that this feeling negatively influenced their adherence behavior, however, this factor was not significantly associated with adherence to the GFD ( $p = 0.445$ ).

Only 11% of the patients responded that they do not have family support to be able to comply with the treatment and 46% of CD patients who have family support considered that family and social events, represent an obstacle in the fulfillment of the diet due to the great offer of gluten-free foods. This situation was significantly associated with the worst adherence to the gluten-free diet ( $p=0.026$ ,  $p < 0.05$ ).

Another barrier in treatment is represented by the lack of availability of gluten-free foods in the market (for 64% of respondents), and two-thirds of the population (71%), considered that the cost of these foods also has a negative impact (Figure 3). However, these factors were not significantly associated with adherence to the GFD ( $p = 0.705$  and  $p = 0.670$  respectively). No person assumed physical impossibilities that prevented him from preparing his own meals, but 39% said he had difficulty doing them for several reasons: not having adequate physical space, kitchen items, lack of time, variety of recipes, lack of will.



Quality of life: The highest scores in the Physical Component Summary (PCS) were found in the physical function of domain ( $82.1 \pm 28.8$ ), followed by physical role ( $73.2 \pm 41.9$ ) (Table 3). The lowest values were determined in the general perception of health ( $45.5 \pm 24.5$ ), being even lower in the age range between 18 and 40 years ( $34.3 \pm 22.0$ ) and in men ( $37.5 \pm 32.3$ ). The

domain of body pain shows values below 50 in all age ranges and in both genders, being lower in the age range between 18 and 40 years ( $21.9$  to  $28.7$ ) and in women ( $24.0$  to  $27.1$ ). For the Mental Component Summary (SCM), the values were above 50 and in energy and vitality, they were lower than 50 in the range of 18 to 40-year-old group ( $37.5 \pm 25.2$ ) and in women ( $41.7 \pm 28.8$ ).

Domain*	Total (n:28)	Age 18-40 y (n:16)	Age + 41 (n:12)	Female (n:24)	Male (n:4)
Physical functioning	$82.1 \pm 28.8$ (71.6-93.0)	$89.1 \pm 20.3$ (81.6-96.6)	$68.9 \pm 35.9$ (54.9-85.1)	$76.0 \pm 34.2$ (63.4-88.6)	$62.5 \pm 41.5$ (47.2-77.8)
Physical role	$73.2 \pm 41.9$	$78.1 \pm 40.7$	$67.1 \pm 44.1$	$76.0 \pm 34.2$	$62.5 \pm 47.9$

	(57.7-88.7)	(63.0-93.2)	(46.7-85.1)	(63.4-88.6)	(44.8-80.8)
Pain	25.0±29.7 (43.7-65.7)	21.9±28.7 (11.3-32.5)	30.0±33.6 (15.7-50.2)	24.0±27.1 (14.0-34.0)	31.3±47.9 (13.6-49.0)
General health perception	45.5±24.5 (36.4-54.6)	34.3±22.0 (26.2-42.4)	60.8±22.8 (47.2-75.7)	46.8±23.6 (38.1-55.5)	37.5±32.3 (25.5-49.4)
Social functioning	71.4±36.4 (57.9-84.9)	84.4±22.1 (76.2-92.6)	55.7±46.3 (27.6-80.5)	72.9±36.1 (59.6-86.2)	62.5±47.9 (44.8-80.2)
Energy/vitality	42.1±30.0 (31.0-53.2)	37.5±25.2 (28.2-46.8)	53.1±33.8 (38.9-65.1)	41.7±28.8 (31.1-52.3)	45.0±41.2 (21.8-60.2)
Emotional Role	64.3±44.8 (47.7-80.9)	78.1±40.7 (63.0-93.2)	43.5±44.8 (13.5-73.1)	64.6±45.4 (47.9-81.3)	62.5±47.9 (44.8-80.2)
Mental Health	45.5±20.9 (37.8-53.2)	49.5±17.2 (43.1-55.9)	41.0±25.5 (30.1-52.6)	48.3±20.6 (40.7-55.9)	47.5±18.9 (40.5-54.5)
PCS	63.5±17.0 (57.2-69.8)	65.1±15.5 (59.0-71.2)	61.9±19.0 (52.4-72.6)	65.3±15.7 (59.5-71.1)	53.1±23.2 (59.5-73.8)
MCS	55.5±19.0 (36.3-62.3)	62.9±14.9 (57.4-68.4)	46.4±18.1 (37.4-58.1)	56.7±18.6 (49.8-63.6)	54.6±20.2 (47.1-62.1)

**Table 3:** Mean values, standard deviation and 95 % confidence interval of the domains of the SF12 questionnaire by age and gender.

\*Data are presented as mean ±SD and confidence interval (95 %). Physical component summary (PCS) included physical functioning (PF), physical role (PR), pain (P), and general health (GH). Mental component summary (MCS) included social functioning (SF), energy/vitality (E/V), emotional role (ER) and mental health (MH)

The MCS showed significant different, between the \_\_\_\_\_ years old (Table 4).  
group of age 18-40 years compared to the group >40

	Physical Component Summary (PCS)	Mental Component Summary (MCS)
Age 18-40 years (n:16)	65.1±15.5 (59.0-71.2)	62.9±14.9 (57.4-68.4)
Age >41 years (n:12)	61.9±19.0 (52.4-72.6)	46.4±18.1 (37.4-58.1)
<b>p Value *</b>	<b>Ns (p &gt;0.05)</b>	<b>Ns (p &gt;0.05)</b>
Female (n:24)	65.3±15.7 (59.5-71.1)	56.7±18.6 (59.5-73.8)
Male (n:4)	53.1±23.2 (59.5-73.8)	54.6±20.2 (47.1-62.1)
<b>p Value*</b>	<b>Ns (p &gt;0.05)</b>	<b>Ns (p &gt;0.05)</b>

**Table 4:** Quality of life: comparison of Physical Component Summary (PCS) and Mental Component Summary (MCS) by age and gender.

\*p Values by T student test

## Discussion

This study aimed to assess the effect of GFD on the micronutrient status, on the quality of life and to evaluate

the factors that influence the GFD adherence of adults with CD.

Although no significance differences (p>0.05) were found in the mean serum concentrations of folate,

magnesium, iron and vitamin B12 between high and low adherence group, almost 46.4 % of CD patients showed low serum folate concentration (<3.1 ng/ml). The deficiency of serum folate was more widespread in those patients who reported high adherence (53.8%) than in those with low adherence (33.3 %). The current observation showed that those patients who follow a strict GFD, have more frequently low serum folate concentration. These results show that the intake of GFD can accentuate nutritional deficiencies that may already be present in patients with CD. Previous reports have shown folate deficiencies in subjects with newly diagnosed disease and even in adults detected by screening [10,11].

CD patients should be advised on the nutritional quality of gluten free food, taking into account that some inadequacies of dietary intake, such as deficient intake of folate, may be originated in the food choice, in addition to inherent deficiencies in GFD. The prevalence of folate deficiency among the celiac patients was quite different from that reported of women of the same range of age in Argentina (53.8 % vs 4 %, celiac patients and adult women, respectively) [12]. Though the sample size is small, these results were in agreement with previous studies that show low folic acid intake in celiac patients when compared with the general population [2,13].

The prevalence of serum vitamin B12 is quite similar to the general population. In Argentina, 49% of pregnant women and 12% of adult women presented low serum vitamin B12 [12]. We observed that 6.6 % of celiac patients have low serum concentration of vitamin B12 (<187 pg/ml).

The prevalence of anemia (14.2%) was in the range of different studies that reported anemia between 12% to 69 % of newly diagnosed patients with CD (hemoglobin concentration < 12 g%) [14]. No differences were observed in the percentage of CD patients with serum iron deficiency (Fe concentration: 65-180 ng/ml) between the group of low and high adherence (6.7 % vs 7.7 %).

Many factors have been assessed through the factors' questionnaire, only difficulty to follow GFD during social events, when dining out, presented significant association ( $p=0.026$ ,  $p < 0.05$ ). The lack of information in the composition of food in restaurant or social meetings could be a negatively influence [15]. The percentage of patients (47 %) that reported high adherence to the diet was quite lower than those observed by us in a previous work

(72.3%; unpublished results); this situation showed some kind of deterioration in the compliance to GFD.

The patients tend to overestimate the level of adherence to GFD, 64 % of patients answered that they follow strictly the treatment in contrast to only 47 % of the same group that expert nutritionists ranked as high adherent. No association was found between the level of adherence to GFD and the serum micronutrients concentration.

54% of patients report eating corn-based foods 3 or more times a week, while in a previous survey only 2.6 to 7.4% of general student population consumes cornmeal [9].

The evaluation of quality of life was acceptable for the PCS ( $63.5 \pm 17.0$ ) but the perception of physical ( $21.9 \pm 28.7$ ) pain and general health perception ( $34.3 \pm 22.0$ ) indicated deterioration especially in the age range of 18 to 40 years. Previous surveys have reported low score of the emotional dimension in the group of CD patients under GFD treatment [16]. The MCS ( $55.5 \pm 19.0$ ) was acceptable. We observed the lowest scores of the emotional role ( $43.5 \pm 44.8$ ) in the group older than 41 years, and the vitality and energy component ( $37.5 \pm 25.2$ ) indicated worsening especially in the age range of 18 to 40 years.

In previous studies, the evidence suggests that the level of compliance to diet is not related to the status of quality of life, although some studies have reported some kind of associations in some domains (perception of health) [17]. In our study, no association was observed between MCS domain and the level adherence to GFD ( $p:0.594 > 0.05$ ).

## Conclusions

The low serum level of folate in both groups of patients, those who adhere to the diet and those who don't, shows the need to increase the consumption of this micronutrient, it is important to consume the appropriate amounts of foods rich in folic acid, such as green leafy vegetables, such as arugula, spinach, endive, lettuce, chard.

Recommendations for dietary supplementation should be reviewed to take these deficiencies into account and to improve the nutritional quality of GF food products and hence the health of CD patients adhering to the GFD.



The health and quality of life of people with celiac disease could be get better with the increment of offer of gluten-free foods in restaurants, markets and food supply locations.

Strategies to disseminate information about this disease in the population are necessary and education programs should be included both for patients and for the medical team and the people who process food.

### Conflicts of Interest

The authors declare no conflict of interest

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