

Health related quality of life in celiac children and adolescents

Calidad de vida relacionada a la salud en niños y adolescentes con enfermedad celíaca

Marianela Rojas^{a,b}, Amaya Oyarzún^b, Jimena Ayala^{b,c}, Magdalena Araya^a

^aPediatric Gastroenterology Program, University of Chile. Chile

^bInstitute of Nutrition and Food Technology, University of Chile, Santiago, Chile

^cSocial worker

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Abstract

The lifelong gluten-free diet (GFD) is the treatment of celiac disease (CD). Being a restrictive diet, it limits daily life and can impact on the health-related quality of life (HRQoL). Our objective was to assess HRQoL of celiac patients on a GFD, the concordance between patients - caregivers, and to compare the local results with international data. **Patients and Method:** Patients aged 8-18 years on a GFD for ≥ 6 months (37 dyads) were evaluated. The "Celiac Disease Dutch Questionnaire" (CDDUX) was applied, which evaluates in two questionnaires (one applied to the child and another one to the caregiver/parent), three areas: i) having CD, ii) communication with others, and iii) the diet. Reliability, dimensionality, and internal consistency were assessed using the Cronbach coefficient. **Results:** More than 50% of patients and caregivers reported "well/very well" on sub-scales "having CD" and "GFD"; "communication" showed high percentages of "bad/very bad". Although there were no significant differences in HRQoL (global and subscale) perceived by patients and caregivers, there were when analyzing the answers of caregivers, who assigned better scores to boys ($p=0.022$) and to patients maintaining a non-strict GFD ($p=0.049$). Concordance between patients and caregivers was 39.2%. **Discussion:** HRQoL of the assessed celiac children was satisfactory, among the best reported in Latin America. "Having CD" and the need for a "GFD" have less influence on HRQoL than "communication" with others about the disease. The concordance found suggests that the caregivers' perception does not necessarily reflect what patients perceive.

Keywords:

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Correspondence:
Magdalena Araya
maraya@inta.uchile.cl

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Introduction

Celiac disease (CD) is a chronic immune-mediated disease triggered by gluten intake in genetically susceptible patients^{1,2}. Although there is no cure, it has highly effective treatment through the gluten-free diet (GFD), which should be strict and on a permanent basis¹. However, keeping this diet implies difficulties for the patient and modifies his/her daily life, for instance, the patient has to modify his/her eating habits, to adapt his/her cultural preferences to the availability in the market, be able to ensure his/her access to safe gluten-free foods on which the information is often insufficient and also are very expensive. Failure to adequately follow the GFD exposes the patient to medical complications, increases morbidity and mortality, and may deteriorate the patient's quality of life^{3,4}. Although there are initiatives that actively seek other non-dietary therapies^{5,6}, to date, this diet is the only available treatment and requires that an important aspect of long-term management focus on supervision and promotion of diet adherence^{7,8}. Blood antibodies measurement (anti-transglutaminase 2 {tTG}, anti-endomysium or anti-deamidated gliadin peptides) has high sensitivity and specificity to make diagnosis in both children and adults, however, evidence obtained in several studies show controversial results about its role in the follow-up of CD, for example, the evolution of the histological lesion is not consistent with serologic results⁹⁻¹¹. When comparing tTG results with in-depth interviews by a nutritionist trained in CD, a study in the United States showed that 30% of the interviewed patients who did not adhere to the diet had negative tTG¹². In the Netherlands, another study showed that 40% of dietary non-compliances may go unnoticed when patients are assessed by serology or by Biagi questionnaire¹³. In our experience, 22% of patients who were classified as adherents in an in-depth interview had positive tTG and 22% of those who classified as non-adherents had negative tTG (submitted for publication, in review 2019). Hence, some authors currently propose that an in-depth interview by a trained professional would be a necessary and complementary way to follow-up the patient, allowing address qualitative as well as quantitative aspects^{14,15}. This demands information about the changes that following the GFD implies in daily life^{7,14} and its repercussions on the patient's quality of life. In our country, there is no information on these subjects and, additionally, they are strongly influenced by local culture, which makes data obtained in other societies not easily applicable to ours.

Health-related quality of life (HRQoL) is a complex and multidimensional concept that, in general terms, refers to the impact of health and disease and/

or their treatments on the individual's quality of life from the perspective of the patient¹⁶⁻¹⁸. There are three HRQoL measurement questionnaires that can be used on children and adolescents. Two are specific for celiac disease, the TACQOLCD¹⁹⁻²¹ and the Celiac Disease Dutch Questionnaire CDDUX²². The TACQOLCD is a questionnaire in which the 'welfare state' of children has been estimated by researchers and physicians ('top-down' methodology), thus it does not provide information from the point of view of children or their parents. It is limited by the fact that it only contains questions related to symptomatology. The CDDUX, developed in the Netherlands, is a bottom-up instrument, in other words, the baseline information for constructing the questions was obtained from the children and their families. Therefore, this questionnaire is considered as 'child-centered' and is designed for children and their parents/caregivers to generate, prioritize, and explain the issues that interest them, thus obtaining data that may even have previously gone unnoticed. As a methodology, it is not aimed at qualifying the state of health or adherence to the gluten-free diet, but to assess the patient's perception of their welfare level. The design is based directly on the generic questionnaire DUX 25 which evaluates HRQoL²². Given how difficult it is to evaluate these aspects, the scarce information in children and, especially in Chile, about HRQoL and CD, the objectives of this work were: i) to measure HRQoL in Chilean celiac patients treated in Santiago (capital city), ii) to determine the concordance between patients and caregivers, and iii) to compare the results with those reported in the international literature.

Patients and Method

Design and study group

Descriptive, cross-sectional study which evaluated the universe of treated patients in the Gastroenterology Polyclinics of the Diagnostic Center (CEDINTA) of the Institute of Nutrition and Food Technology (INTA), University of Chile, *Hospital Roberto del Río*, and *Hospital Militar*, between October 2016 and March 2018. Children of both sexes, aged between 8 and 18 years were evaluated, whose celiac disease diagnosis included a duodenal biopsy, and followed GFD for at least 6 months. The lower age limit was set at 8 years as the minimum age for proper reading and comprehension of the questionnaire. Neither the child nor the parent/caregiver had chronic illnesses or mental or physical conditions that could interfere with the interview and answer the questionnaire. In order to characterize the study group, the following data were recorded: the age and sex of the patient,

the relationship with the caregiver who answered the survey, region of residence, health care system, family members, and educational level of the caregiver. The protocol was accepted by the Ethics Committee of INTA. Patients and caregivers signed an informed consent/assent according to age.

The HRQoL (Health-Related Quality of Life) measurement instrument

This questionnaire, specific to CD, was translated, adapted, and validated in Argentina and includes two versions, one for children and another one for parents/caregivers^{22,23}. The instrument measures the quality of life through the identification of different emotions expressed in five facial expressions, considering that the visualization of facial expression is more identifiable with a certain feeling, which could be long and difficult to define globally in words (Tables 1 and 2). It gathers information in three areas, summarized in the following three subscales: i) *having CD* (how the child feels when offered gluten-containing food or when he/she thinks of gluten-containing food, questions 1, 2, and 10), ii) *communicating with others* (how the child feels when talking about celiac disease with others and/or explaining it to others, questions 3, 6, and 7), and iii) *the diet* (how the child feels about diet adherence and restrictions, and all aspects of his/her life, questions 4, 5, 8, 9, 11, and 12). In the case of the caregiver, the questions are interpreted as the caregiver's appreciation of how the child feels in each of the addressed situations. For children/adolescents and for parents/caregivers, the self-administered version was used. The 5 options of facial expressions are interpreted as very bad, bad, neutral, good, and very good. The person must mark the one that best represents his or her feelings facing the situation posed by the question. The instrument addresses 12 items grouped into the three subscales (6), each 'face' assigns 1 to 5 points, from the saddest (1 point) to the happiest (5 points) (five-point Likert scale), and the sum of the answers gives a final score, on a scale of 1 to 100. The higher scores indicate better quality of life (1 to 20: very bad, 21 to 40: bad, 41 to 60: neutral, 61 to 80: good, 81 to 100: very good).

Procedures

After identifying and inviting the families (patient and caregiver) during a routine consultation, those families who agreed to participate signed an informed consent/assent before the evaluation. They were scheduled for an interview, where a first questionnaire was applied, which collected general socio-demographic, and diagnostic data on CD, and the CDDUX questionnaire^{22,23}. Patients and their caregivers answered the surveys separately.

Result analysis

The Cronbach's coefficient was calculated for reliability and dimensionality, and the internal consistency for the full scale of 24 items (12 patients and 12 caregivers). The Student t-test was used to compare the mean scores of the questionnaires applied to the children and their parents/caregivers. ANOVA was used to verify the variance of patient means in relation to gender, age (older or younger than 11 years), region of residence (MR vs. other), GFD duration (more or less than 5 years), and declaration of strict GFD adherence (strict vs. not strict). In addition, the opinion concordance of children with their parents was analyzed through the kappa statistics. A value of $p < 0.05$ was considered significant for the analyses. The statistical software SPSS 14.2 for Windows was used.

Results

74 individuals were evaluated, corresponding to 37 caregiver-child dyads. Table 3 shows the socio-demographic characteristics. 40.5% of participants present a GFD adherence for more than 5 years, and regarding how they follow the diet, 59.5% declared that they followed it strictly. In 94.6% of the cases, the school staff was aware of the child's diagnosis, however, according to the caregiver's appreciation, only 35.1% know about celiac disease and the requirements of its treatment. More than 50% of patients and their caregivers report good/very-good on the subscales 'having the disease' and 'maintaining the gluten-free diet' but not on 'communication', which showed the highest percentages of bad/very bad responses. Figure 1 shows the distribution of patient and caregiver answers in the three evaluated areas. No significant differences were found between patients and caregivers. When expressing the answers in extreme groups (bad/very bad, neutral, and good/very good), the comparison between children and their caregivers showed significant differences in the subscale GFD, with a higher percentage of bad/very bad score in patients (24.3%) than in caregivers (17.1%). Out of the 12 patients who self-reported as bad and very bad, 8 were classified differently by caregivers, 4 as neutral, and 4 as good or very good (% concordance=35.14%, $p = 0.0426$).

Quality of life

There were no significant differences between the HRQoL perceived by patients and their caregivers, both in the overall score and by subscale (table 4). When analyzing patient answers, the variables sex, age (older or younger than 11 years), region of residence (MR vs. other), GFD duration (more or less than 5 years), declaration of strict GFD adherence (strict vs. not strict), there were no significant differences in the overall score of

Table 1. CDDUX questionnaire applied to patients

We are interested in knowing how you feel lately. Please mark how you feel in the following situations
Circle the face that represents better how you feel

There are no incorrect answers. What is important is how you feel about it.

Indicate how you feel lately

1	When I think of food containing gluten, I feel ...					
2	When at school I am given food containing gluten, I find it...					
3	Talking about celiac disease I find...					
4	Not being able to eat anything I want, I feel ...					
5	When someone offers me food containing gluten, I feel ...					
6	Explaining to others what celiac disease is, I find it...					
7	Talking about celiac disease to others my age, I feel...					
8	Following a lifelong diet, I find it...					
9	Having to pay attention to what I eat, I find ...					
10	Having celiac disease is ...					
11	Not being able to eat all the things other people eat, I find it...					
12	Following a diet for my celiac disease is...					

¡Gracias por tus respuestas, hasta pronto!

Table 2. CDDUX questionnaire applied to caregivers

We are interested in knowing how your son/daughter feels lately.
Please mark how your son/daughter feels lately, in the following situations
Circle the face that represents better how you feel.

There are no incorrect answers. What is important is your opinion.
Indicate how your son/daughter feels lately

1	When your son/daughter thinks of food containing gluten, he/she feels ...					
2	When at school they offer him/her food containing gluten, he/she feels					
3	Talking with others about his/her celiac disease, he/she feels ...					
4	Not being able to eat anything, he/she feels ...					
5	When someone offers him/her food containing gluten, he/she feels ...					
6	When your son/daughter has to explain what is celiac disease, he/she feels ...					
7	When he/she talks about celiac disease with others of his/her age, he/she feels ...					
8	Following a lifelong diet, he/she finds it...					
9	Having to pay attention to what he/she eats, he/she feels ...					
10	Having celiac disease is ...					
11	Not being able to eat all the things other people eat, your son /daughter finds it...					
12	Following a diet for his/her celiac disease, your son/dughter finds it...					

HRQoL or in the subscales. In caregiver responses, the overall HRQoL score was better in male patients (73.4 v/s 61.5, $p = 0.022$) and in those who followed GFD non-strictly (73.9 v/s 63.3, $p = 0.049$). On the GFD subscale, scores were higher for males (77.0 v/s 64.4, $p = 0.04$) and for those older than 11 years (76.5 v/s 63.5, $p = 0.035$).

Concordance

HRQoL concordance analysis reported by patients and caregivers showed agreement on 39.2%. In the concordance analysis of each question, eight present kappa values in the acceptable category (kappa 0.20-0.40) and in 4 questions, the kappa concordance values are mild (kappa < 0.20) (below average concordance percentages) ['When I think of gluten-containing food I feel' (24.32%, kappa = 0.03), 'Talking to other children/adolescents about their life is' (32.43%, kappa = 0.1224), 'When I have to explain to others what celiac disease is, I feel' (35.14%, kappa = 0.1494), and 'Following the diet for me is' (24.32%, kappa = 0.0309)].

Table 3. General characteristics of 37 dyads evaluated for health quality of life in celiac disease

Variables		n	%
Age of patient	≤ 11	16	43.2
	> 11	21	56.8
Relation to caregiver	Mother	32	84.5
	Grandmother	1	2.7
	Father	4	10.8
Sex of patients	Girls	18	48.6
	Boys	19	51.4
Residence	City	19	51.4
	Others	18	48.6
Health insurance	Public	22	59.5
	Private	12	32.4
	None	3	8.1
Number of family members	2 a 3	6	16.2
	4	21	56.8
	5 a 6	9	24.3
	10	1	2.7
Schooling (caregivers)	< 8 years	4	10.8
	8 years	4	10.8
	12 years	12	32.4
	> 12 years	17	45.9

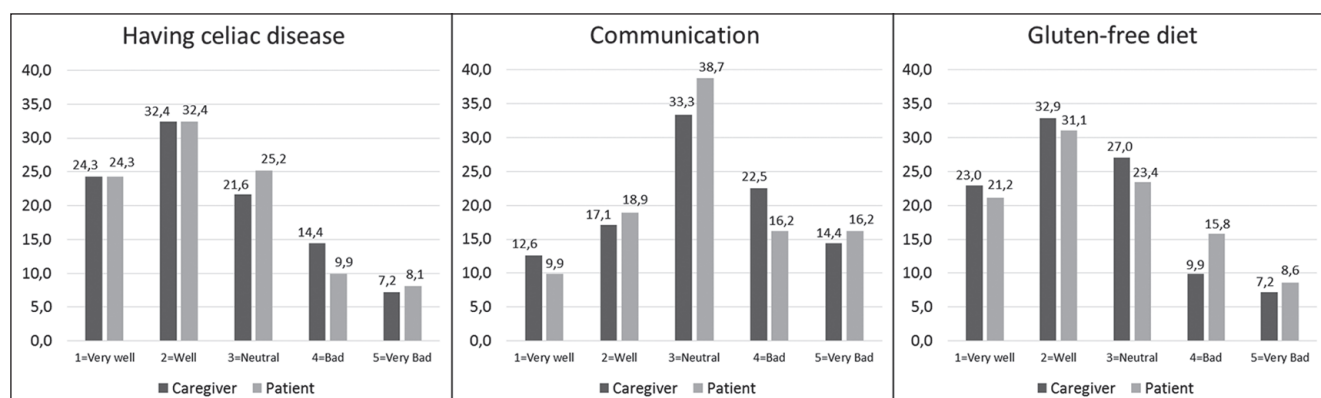


Figure 1. Patients and caregivers' responses in the categories "having CD", communication with others, and the gluten-free diet, expressed as percentages of responses classified as very well, well, neutral, bad and very bad.

Table 4. Scores obtained by celiac patients in different countries, assessed by Celiac Disease Dutch Questionnaire (CDDUX)

Domain /Score		Chile 2018 (n = 37)	Spain 2016 (children=26, parents=428)	Iran 2016 (n = 65)	Brazil 2015 (n = 33)	Argentina 2012 (n = 193)	Holland 2008 (n = 510)
		Mean ± DS	Mean ± DS	Mean ± DS	Mean ± DS	Mean ± DS	Mean ± DS
Patients	Having CD	70.3 ± 18.2	46.5 ± 13.1**		44 ± 13.8	55.3 ± 17.2	36 ± 21*
	Communication	58 ± 21.1	72.0 ± 16.9		71.3 ± 18.1**	76.0 ± 21.0	59 ± 21*
	GFD	68.1 ± 17.4	51.7 ± 17.0		57.6 ± 16.7**	65.1 ± 17.9	36 ± 16*
	CDDUX	66.1 ± 15.3	55.5 ± 12.7	30.2 ± 15.0**	57.6 ± 12.3**	64.9 ± 14.4	44 ± 15*
Caregivers	Having CD	70.5 ± 16.1	49.8 ± 12.6		45.4 ± 14.3	51.5 ± 14.5	30 ± 18
	Communication	58.2 ± 22.6	69.6 ± 15.7		38.4 ± 10.7	64.1 ± 18.4	53 ± 20
	GFD	70.9 ± 18.8	50.0 ± 15.7		52.3 ± 14.1	55.4 ± 17.1	33 ± 18
	CDDUX	67.6 ± 16.1	54.8 ± 12.3	25.2 ± 14.4	45.4 ± 10.4	56.6 ± 14.1	39 ± 15

Values indicate (health) quality of life (range 0-100) 1 to 20 = very bad, 21 to 40 =bad, 41 to 60 =neutral, 61 to 80 =well and 81 to 100 =very well. * $p < 0.05$.

The quality of life of the pediatric celiac patient. Chile versus other countries

The literature review revealed only five additional studies, which use the methodology that includes the appreciation of the patient him/herself and the caregiver's opinion (table 4). Comparative analysis showed that the patient's appreciation differs from that of the caregiver in Spain, Iran, Brazil, and the Netherlands, unlike Chile and Argentina, where differences do not reach statistical significance.

Discussion

The results show that more than 50% of patients and their caregivers report that they are good/very good on the subscales 'having the disease' and having to 'maintain the gluten-free diet', suggesting that they have learned to manage both the fact of having (or being) a chronic patient in the family and the need to maintain a restrictive diet as a treatment. In contrast, the highest percentages of bad/very bad responses are on the subscale 'communication', showing that the dyad finds it difficult to maintain communication with others. In this subscale, the high percentage of neutral responses is striking, which, in the area of coping with chronic diseases, is interpreted as indifference. It is well known that chronic diseases affect the HRQoL, which is difficult to measure because in the evaluation influences the daily experience of eating and relating with others, which varies over time²⁴. If the experience is positive, the emotion that appears is of welfare, while if it is negative, it is associated with discomfort. Neutral answers may reflect uncertainty about gluten-free eating when you are with others, and the emotions that appear will depend on past experiences. Studies in other countries^{22,23,25-27} (table 4) show that, contrary to what we found, the subscale that has the best score is communication. We could interpret these findings as saying that in our country there are health care actions that allow having a basic knowledge of the disease and its treatment (GFD), however, they are insufficient in the communication area. The information generated by the National Socioeconomic Characterization Survey (CASEN) supports this. According to 2015 data, only 0.3% of the population participates in self-help groups in health²⁸. In the networks and social connection dimension, the indicator of social support and participation is 6.1% at the national level out of 7.1% in the metropolitan region, which reflects the low level of social interaction of the Chilean population²⁹. In quality of life and social support studies, quality of life scores were higher for those that only used 'face-to-face' social support compared with 'online assistance' (72.6 vs 66.7; $p < 0.0001$). Longer duration of face-to-

face social support use was associated with a higher quality of life scores ($p < 0.0005$)³⁰.

Cultural factors (micro-social level) and public policies (macro-social level) influence the results obtained in different countries. In the total valuation of the questionnaire, the Chilean values are the highest among the 6 countries analyzed and compared with those reported in Argentina (66.1 and 64.9, respectively) (table 4). However, the concordance between patients and caregivers was lower in our study (39.2%) compared with what was reported in Argentina (64%)³¹. Interestingly, caregivers' responses showed significant differences when analyzed by sex, where the overall CDDUX score reflects their perception that males have better HRQoL. In the Quality of Life and Health Survey (ENCAVI 2016)³² in populations over 15 years of age, 63.8% of women reported having a good/very good quality of life compared with 71.1% of men. This self-perception referring to quality of life, in general, could be transferred to the caregivers' opinion of this study (61.5% women) regarding the patients' HRQoL. The caregiver score was also higher in the group of children over 11 years of age. It may be interpreted as that the older child has better capacities to become aware and decide on his or her self-care, and this could be perceived by the caregiver as his or her HRQoL is better.

When asking directly if the patient is dieting, 78.6% of caregivers say they are. It is remarkable, then, that 21.4% of caregivers recognize that GFD is not followed properly, while it represents the treatment of the disease and must be strict and for life. The school role deserves a special comment. The results show that, although schools know the diagnosis of the child (94.6%), 35.1% are not clear on how to support the patient and his/her family in the treatment with GFD, which makes it difficult for the school to act as the institution that provides assistance and social support to the celiac patient, who as a chronic patient requires long-term support. This point is relevant considering the long school day (8 hours per day) of our country. Initiatives such as the 'celiac PAE' (National feeding program for vulnerable school age children) approach the problem from the material side, offering safe gluten-free foods. There are several studies that show that society's general ignorance of what it means to have CD is another important barrier to dietary compliance. They agree on the importance of promoting and supporting social support strategies based on a comprehensive understanding of the estrangement and marginalization experiences that celiac patients experience in their social relationships through food³³⁻³⁵.

In summary, the results show that the HRQoL of the evaluated celiac children appears as one of the best reported in our region. The low concordance detec-

ted, especially in communication, indicates that the caregivers' perception is not a proxy of the patients' opinion, and this is relevant since they are the ones who usually give the information during follow-up visits of celiac children. These findings emphasize the need to establish a model of comprehensive care that includes the family and the school, in order to improve understanding, support, communication and, therefore, the HRQoL of children and adolescents with celiac disease.

Ethical Responsibilities

Human Beings and animals protection: Disclosure the authors state that the procedures were followed according to the Declaration of Helsinki and the World Medical Association regarding human experimentation developed for the medical community.

Data confidentiality: The authors state that they have followed the protocols of their Center and Local regulations on the publication of patient data.

Rights to privacy and informed consent: The authors have obtained the informed consent of the patients and/or subjects referred to in the article. This document is in the possession of the correspondence author.

Conflicts of Interest

Authors declare no conflict of interest regarding the present study.

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