applied sciences

MDPI

Article

Time Following a Gluten-Free Diet, Ultra-Processed Food Consumption and Quality of Life in Children with Celiac Disease

Rafael Martín-Masot [1,2], Ana Labella [3], Laura Baena-García [4,5,6], Marta Flor-Alemany [2,7], Magdalena López-Frías [2,7,*], Magdalena de la Higuera [8], José Maldonado [3,6,9,10] and Teresa Nestares [2,7]

1 Pediatric Gastroenterology and Nutrition Unit, Hospital Regional Universitario de Malaga, 29010 Málaga, Spain
2 Institute of Nutrition and Food Technology "José Mataix Verdú" (INYTA), Biomedical Research Centre (CIBM), University of Granada, Armilla, 18071 Granada, Spain
3 Pediatric Clinical Management Unit, "Virgen de las Nieves" University Hospital, 18014 Granada, Spain
4 Sport and Health University Research Centre (iMUDS), University of Granada, Armilla, 18071 Granada, Spain
5 Department of Nursing, Faculty of Health Sciences, University of Granada, 51001 Ceuta, Spain
6 The Institute of Biomedicine Research (Instituto de Investigación Biosanitaria, ibs), 18014 Granada, Spain
7 Department of Physiology, Faculty of Pharmacy, University of Granada, 18071 Granada, Spain
8 Department of Endocrinology and Nutrition, Clínica Universidad de Navarra, 28027 Madrid, Spain
9 Department of Pediatrics, School of Medicine, University of Granada, 18071 Granada, Spain
10 Primary Care Interventions to Prevent Maternal and Child Chronic Diseases of Perinatal and Developmental Origin (RICORS), Carlos III Health Institute, 28029 Madrid, Spain
* Correspondence: maglopez@ugr.es; Tel.: +34-958243880

Citation: Martín-Masot, R.; Labella, A.; Baena-García, L.; Flor-Alemany, M.; López-Frías, M.; de la Higuera, M.; Maldonado, J.; Nestares, T. Time Following a Gluten-Free Diet, Ultra-Processed Food Consumption and Quality of Life in Children with Celiac Disease. *Appl. Sci.* **2022**, *12*, 11680. https://doi.org/10.3390/app122211680

Academic Editor: Wojciech Kolanowski

Received: 10 October 2022
Accepted: 14 November 2022
Published: 17 November 2022

Featured Application: The data from the present study indicate that nutritionists and other health-care professionals should monitor the quality of life and diet quality of children with celiac disease, especially from the first year of treatment with a gluten-free diet.

Abstract: Maintaining a strict gluten-free diet (GFD) may affect the quality of life of children with celiac disease (CD) and promote a less healthy diet by substituting gluten-containing foods with ultra-processed foods. We aimed to assess the influences of the GFD and ultra-processed food consumption on parents' perception of the quality of life of children with CD. Fifty-eight children (mean age 8.6 ± 4.1 years) were included. The participants were divided into groups based on the time following a GFD: <6 months (n = 18) versus ≥12 months (n = 37). Their dietary consumption was assessed through a three-day food record. The 20-item Celiac Disease Quality Of Life survey (CD-QOL), which contains four subscales (limitations, dysphoria, health concerns, and inadequate treatment) was used to assess the quality of life. The children who followed a GFD for ≥12 months presented poorer scores in the limitations subscale than those who followed a GFD for <6 months (p = 0.010). The mean % of the energy intake from ultra-processed foods was 47.3 ± 13.5. Children with CD consuming more than 50% of their total energy from ultra-processed foods showed poorer scores for the limitation and inadequate treatment (both, p = 0.019) subscales than their counterparts. According to parents' perceptions, those children who consumed more than 50% of their energy through ultra-processed foods had more limitations, and their treatment was perceived as less effective.

Keywords: childhood; celiac; diet quality; energy intake; fast food; food processing; gluten; limitations

1. Introduction

Celiac disease (CD) is a multifactorial and chronic enteropathy caused by an immune reaction following exposure to gluten ingestion in genetically predisposed individuals [1]. Generally, patients diagnosed with CD present with several signs and symptoms, such as anemia, diarrhea, abdominal pain and bloating, osteomalacia, and osteoporosis, among others [2]. In recent decades, the incidence of CD has significantly increased in industrialized

countries [3], and currently, a strict gluten-free diet (GFD) is the only effective treatment for CD. Adherence to a GFD usually reduces the symptoms and intestinal damage [4]. However, the chronicity of this disease and the difficulties associated with having a permanently restrictive diet can affect the quality of life of CD patients and their families [5,6]. One of the main impediments to adherence to the GFD could be the social and economic difficulties involved in following this diet [7], which can cause low self-esteem, leading to a deterioration in the quality of life and psychological problems [8]. Low adherence to the GFD has been described as one of the main factors associated with the prevalence of psychological disorders in these patients [9].

Ultra-processed foods (UPF) are products of food technology that contain at least five industrial ingredients, most which which have lower costs and nutritional values [10]. UPFs containing little or no whole food [11] have high caloric contents (up to 500 kcal/100 g) and a low nutritional quality, as well as a high glycemic load, because they are rich in sodium, simple sugars, and saturated and trans fats, and low in fiber, proteins, and various micronutrients, and because they contain a large number of additives in order to resemble natural foods as closely as possible [10,12]. It should be noted that several components of UPFs make them highly attractive and addictive, similar to some types of drugs [13]. Some studies correlated the consumption of UPFs with an increased prevalence of chronic diseases during childhood and adulthood [10,14–16] and even with depression in adult populations [17].

The scientific literature raises questions concerning the food choices of individuals with CD, because they substitute natural gluten-containing products with their ultra-processed gluten-free analogs [10]. This can have a negative effect on health, and it should be seriously taken into account, since the limited choice of food products for the diets of children with CD can induce a high consumption of UPFs, such as snacks and biscuits. In this sense, we previously reported that children with CD consumed more UPFs compared with children without a diagnosis of CD in our study sample [18]. Furthermore, among the children with CD, those who had a lower intake of UPFs showed a better inflammatory signaling and oxidative status [18]. Therefore, we aimed to explore the association between the time following a GFD and UPF consumption and the quality of life of children with CD.

2. Materials and Methods

2.1. Subjects

This study included 58 children aged 7–18 years old and their parents using the Gastroenterology, Hepatology, and Child Nutrition Service of the "Virgen de las Nieves" University Hospital in Granada (Spain).

CD children diagnosed according to the European Society for Pediatric Gastroenterology Hepatology and Nutrition (ESPGHAN) criteria [19] were included in the study. As previously described [19], the exclusion criteria were inflammatory bowel disease, inflammatory pathologies, hepatic or renal diseases, chronic asthma, diabetes mellitus, and the consumption of dietary supplements with antioxidant actions. We also excluded patients with obesity, following the International Task Force criteria [18]. All the parents signed an informed consent form that included the aims and procedures of the study. Moreover, they completed all the assessments and provided the data collected for the present study.

The participants were grouped according to the time following a GFD, including less than 6 months (GFD < 6 m) (n = 18) and more than 12 months (GFD > 12 m) (n = 37).

The Ethics Committee of the University of Granada (ref. 201202400000697) approved this study, and the principles of the Declaration of Helsinki and its later amendments were followed.

2.2. Sociodemographic and Clinical Characteristics

Socio-demographic (such as age, parents' marital status, and educational level) and clinical (smoking habits and previous diseases) data were collected through a self-administered survey. The parents were instructed by the research team to complete it properly.

2.3. Dietary Assessment

We assessed the dietary intake through a three-day record (two on weekdays and one on weekends). To ensure the correct handling of the dietary diary, the participants were given instructions and a photographic atlas including different portion sizes and a set of household measures [20], and a trained dietitian carefully explained the procedure to the children and their parents. The survey was completed for all the meals eaten throughout the day by exhaustively describing the amount of food consumed (using the photographic atlas as a guide), the recipes, and the way it was prepared (method of cooking used, amount and type of fats and sugars added), as well as the brands of the packaged foods consumed.

The above-mentioned dietitian used the Evalfinut software, which includes the Spanish Food Composition Database [21], to obtain reference values for the energy and food group consumption and to analyze all the daily diaries. In this way, the energy intake (kilocalories) and macronutrient (total fats, saturated fats, proteins, carbohydrates, simple sugars, and fiber, expressed in grams) intake, as well as the calorie percentage of each macronutrient, were estimated. The exact composition of the gluten-free products was obtained from the information provided on the labels.

We used the NOVA classification, which categorizes foods according to the degree and purpose of industrial processing, into the following four groups: unprocessed or minimally processed foods; processed culinary ingredients; processed foods; and ultra-processed foods [22]. This is the most widely used method for examining diets according to food processing and has been widely used by international agencies such as the PAHO, WHO, and FAO [12,23,24].

2.4. Quality of Life Assessment

A translation of the 20-item Celiac Disease Quality Of Life survey (CD-QOL) [25] was completed by the parents to assess the children's quality of life. The responses are divided based on a 5-point Likert scale, where 1 = not at all, 2 = slightly, 3 = moderately, 4 = quite a bit, and 5 = a great deal. All the elements of the CD-QOL are negative (e.g., I feel depressed because of my disease), with one exception ("I feel the diet is sufficient treatment for my disease"). We reversed the negative items and then calculated the score of the CD-QOL questionnaire by adding the scores of each question. For example, since the score for each element could range from 1 to 5, a score of 4 ("a great deal") for the element "I feel limited by this disease" was converted to a 1. Finally, an overall score and four clinically relevant scales were obtained after combining all the answers: dysphoria (4 items), limitations (9 items), health concerns (5 items), and inadequate treatment (2 items). The scores range from 10 to 100, with greater scores indicating a better quality of life.

2.5. Data Analyses

Descriptive statistics (number of participants (%) for categorical variables and mean (standard deviation) for quantitative variables) were employed to describe the participants' baseline characteristics. Furthermore, the chi-square test was employed to explore differences in the categorical variables.

Analyses of covariance (ANCOVA) were employed to assess differences in the quality of life total scores and quality of life domains between the CD children who followed a GFD for less than 6 months versus children with CD who followed a GFD for at least 12 months after adjusting for age, sex, and parental working status.

In order to explore the association between the % of the total energy from UPFs, quality of life total scores, and quality of life domains, we performed linear regression analyses after adjusting for age, sex, the number of months following a GFD, and parental working status. Differences in the quality of life total score sand quality of life domains between the CD children based on the % of total energy from UPFs (below 50% vs. above 50%) were assessed with an ANCOVA after adjusting for age, sex, and parental working status.

The statistical analyses were conducted using SPSS 22.0 (IBM, New York, NY, USA). The statistical significance was set at $p < 0.05$.

3. Results

The baseline characteristics of the study sample are shown in Table 1. A total of 58 children with CD participated in the study (mean age 8.6 ± 4.1 years). A total of 18 participants (i.e., 31% of participants (mean age: 5.7 ± 3.8 years)) with CD followed a GFD for less than 6 months. A total of 37 participants (i.e., 64% of participants (mean age: 10.1 ± 3.4 years)) with CD followed a GFD for less than 12 months. Three children followed a GFD for more than 6 months and less than 12 months. Among the 58 children included in this study, 41 participants had valid data in terms of the three-day food record and, therefore, the UPF consumption. The mean % of the total energy from UPFs was 47.3%.

Differences in the quality of life total scores and quality of life domains between the children with CD who followed a GFD for <6 m (n = 18) versus children with CD who followed a GFD for >12 m (n = 37) are shown in Figure 1. After adjusting for age, sex and parental working status, the children who followed a GFD for >12 m had higher limitations than those who spent less time on a GFD (GFD < 6 m) ($p = 0.010$).

The linear regression analysis assessing the quality of life total scores, quality of life domains, and the % of the total energy from UPFs among the children with CD is shown in Figure 2. After adjusting for sex, age, the number of months following a GFD, and parental working status, a greater intake of energy from UPFs was related to greater limitations ($\beta = -0.380$, $p = 0.032$).

The differences in the quality of life total scores and quality of life domains between the children with CD based on the percentage of the energy intake from UPFs (n = 41) are shown in Figure 3. Those children with CD whose % of total energy from UPFs was above 50% presented (n = 16) with more limitations ($p = 0.019$) and inadequate treatment ($p = 0.019$) compared to their counterparts (n = 25). Although it was non-significant, the children with CD who consumed more than 50% of their total energy from UPFs had lower quality of life total scores than their counterparts ($p = 0.067$).

Table 1. Sociodemographic and clinical characteristics of the study participants.

Variable	N	Mean (SD)
Age (years)	58	8.6 (4.1)
Total energy from ultra-processed foods (%)	41	47.3 (13.5)
		n (%)
Sex (female)	58	35 (60.3)
Following a gluten-free diet for at least 6 months	58	18 (31.0)
Following a gluten-free diet for at least 12 months	58	37 (63.8)
Parents' marital status (married)	43	42 (97.7)
Passive smoker	43	3 (7.0)
Living with their parents	43	42 (97.7)
Mothers' working status	58	
Unemployed		6 (10.3)
Employed		52 (89.7)
Fathers' working status	58	
Unemployed		2 (3.4)
Employed		56 (96.6)

Data are given as the mean (SD) unless otherwise stated (i.e., n, %). SD, standard deviation.

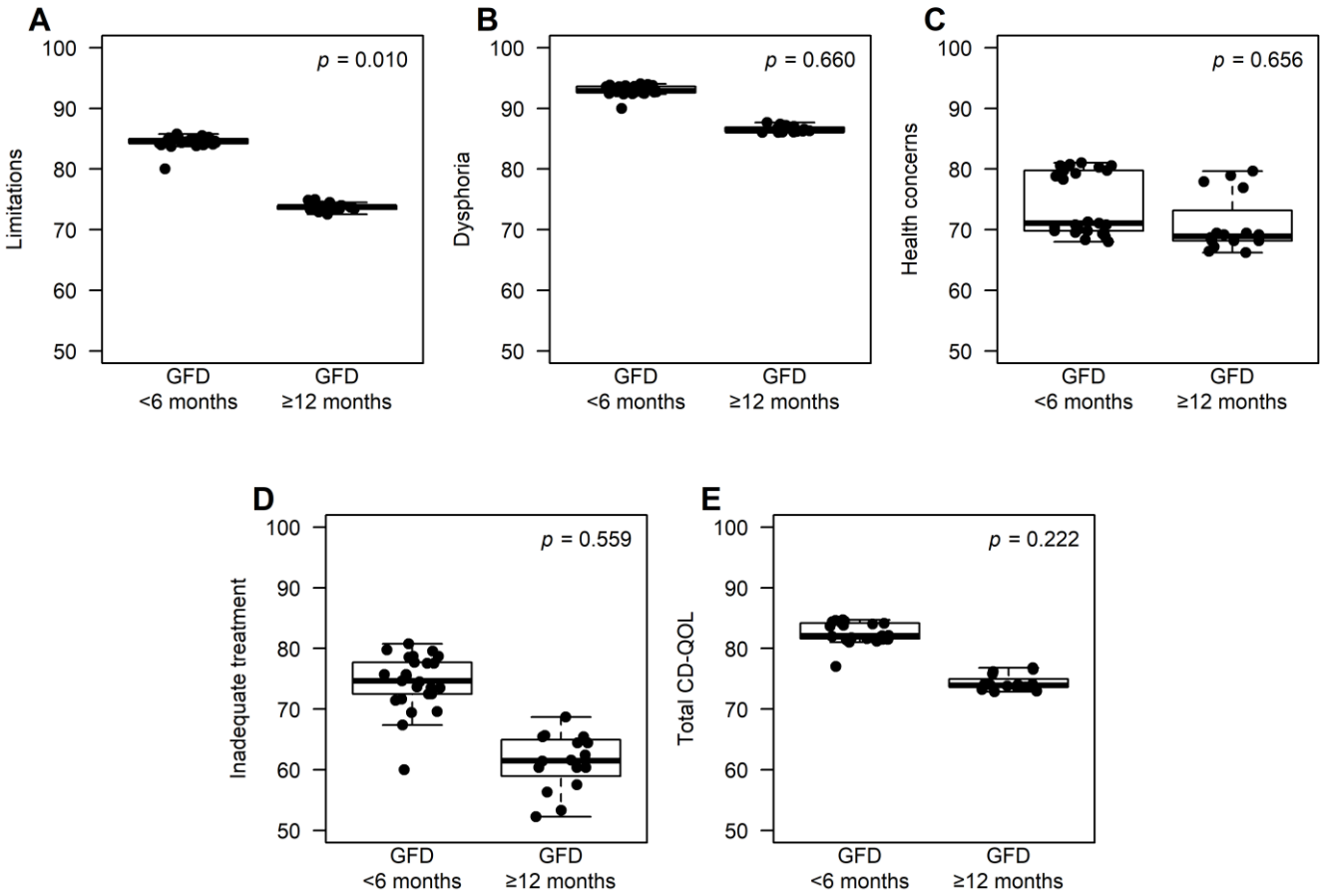

Figure 1. Quality of life total scores and quality of life domains between children with celiac disease following a gluten-free diet for less than 6 months (n = 18) versus children with celiac disease following a gluten-free diet for more than 12 months (n = 37). (**A**). Differences between children with celiac disease following a gluten-free diet for less than 6 months versus children with celiac disease following a gluten-free diet for more than 12 months in the limitations subscale. (**B**). Differences between children with celiac disease following a gluten-free diet for less than 6 months versus children with celiac disease following a gluten-free diet for more than 12 months in the dysphoria subscale. (**C**). Differences between children with celiac disease following a gluten-free diet for less than 6 months versus children with celiac disease following a gluten-free diet for more than 12 months in health concerns subscale. (**D**). Differences between children with celiac disease following a gluten-free diet for less than 6 months versus children with celiac disease following a gluten-free diet for more than 12 months in the inadequate treatment subscale. (**E**). Differences between children with celiac disease following a gluten-free diet for less than 6 months versus children with celiac disease following a gluten-free diet for more than 12 months in the total quality of life. Values shown as the marginal mean (standard error of the mean). Model adjusted for age, sex, and parental working status. CD-QOL, celiac disease-related quality of life (QOL). Greater scores indicate a better perception of each CD-QOL item (e.g., greater scores for the limitations subscale indicate lower self-perceived limitations).

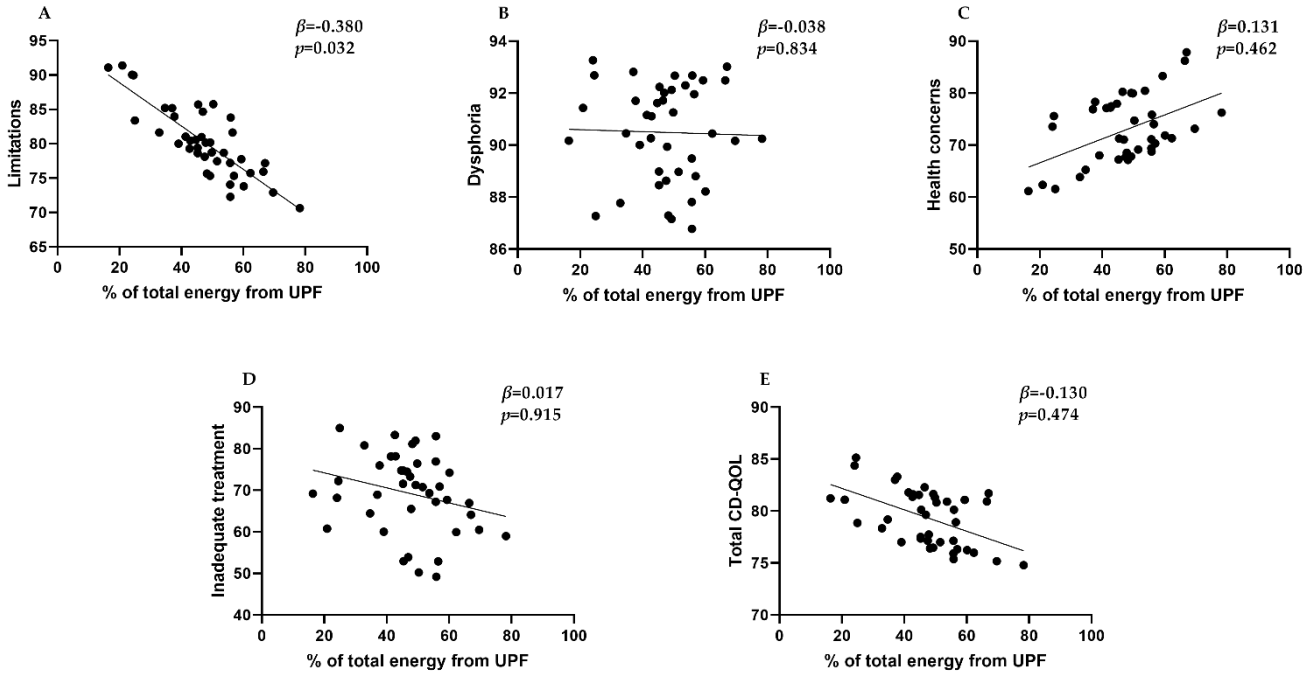

Figure 2. Linear regression assessing the association between the quality of life total scores, quality of life domains, and the % of the total energy from ultra-processed foods in children with celiac disease (n = 41). (**A**). Association between the limitations subscale and % of total energy from ultra-processed foods. (**B**). Association between the dysphoria subscale and % of total energy from ultra-processed foods. (**C**) Association between the health concerns subscale and % of total energy from ultra-processed foods. (**D**) Association between the inadequate treatment subscale and % of total energy from ultra-processed foods. (**E**) Association between the total quality of life and % of total energy from ultra-processed foods. Model adjusted for age, sex, the number of months following a gluten-free diet, and parental working status. CD-QOL, celiac disease-related quality of life (QOL); UPF, ultra-processed foods. Greater scores indicate a better perception of each CD-QOL item (e.g., greater scores for the limitations subscale indicate lower self-perceived limitations). Beta coefficients refer to the standardized (regression) coefficients.

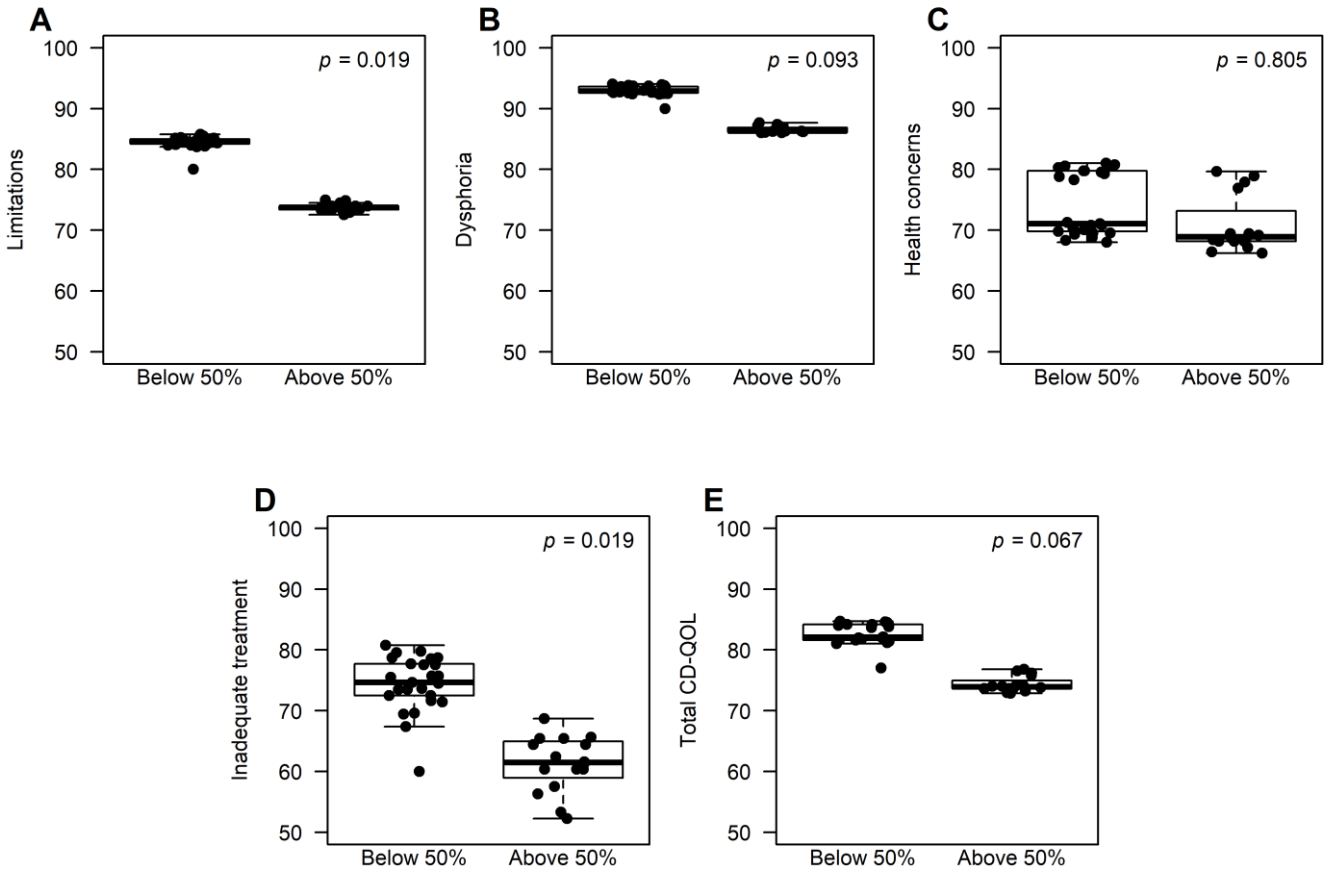

Figure 3. Differences in quality of life total scores and quality of life domains among children with celiac disease based on the percentage of total energy from ultra-processed foods (below 50% vs. above 50%). (**A**) Differences in limitations subscale based on the percentage of total energy from ultra-processed foods (below 50% vs. above 50%). (**B**) Differences in dysphoria subscale based on the percentage of total energy from ultra-processed foods (below 50% vs. above 50%). (**C**) Differences in health concerns subscale based on the percentage of total energy from ultra-processed foods (below 50% vs. above 50%). (**D**) Differences in inadequate treatment subscale based on the percentage of total energy from ultra-processed foods (below 50% vs. above 50%). (**E**) Differences in quality of life total scores based on the percentage of total energy from ultra-processed foods (below 50% vs. above 50%). Values shown as the marginal mean (standard error of the mean). Model adjusted for age, sex, and parental working status. CD-QOL, celiac disease-related quality of life. Greater scores indicate a better perception of each CD-QOL item (e.g., greater scores for the limitations subscale indicate lower self-perceived limitations).

4. Discussion

The main finding of this study was that, according to their parents' perceptions, children with CD who followed a GFD for more than 12 months had more limitations compared with children who followed a GFD for less than 6 months. In addition, according to the dietary records and parental perception, those children who consumed more than 50% of their energy through UPFs had more limitations, and their treatment was perceived as less effective.

On the one hand, the initiation of the GFD can reduce CD symptoms [25] and thus improve the quality of life, but on the other hand, the negative effects on emotional and social areas resulting from following this type of restrictive diet can counteract the initial positive effect. In this sense, a literature review of a sample of 2728 patients with CD highlighted that the GFD significantly improved, but did not normalize, their quality of life [26]. This result is in line with the findings of our study, in which the overall quality

of life was not altered, but more limitations were observed in the patients who followed a GFD for a longer time. These limitations were explored using the CD-QOL questionnaire by asking the patient whether he/she feels limited by the disease, especially concerning social relationships, feels that his/her disease prevents him/her from having a normal life, and feels afraid of food containing gluten, etc. [25]. As the time spent with the illness increases, the quality of life can be affected by the changes resulting from having a chronic disease and the difficulty of having a higher adherence to this strict diet [27]. In fact, a previous study showed that patients who were asymptomatic at diagnosis had a worse quality of life several years after diagnosis than those who had symptoms. Therefore, the CD symptomatology is not the only factor associated with a poorer quality of life [7]. Other studies concluded that the quality of life of people with CD is related to the age at diagnosis, with better adaptation when the disease is detected at an earlier age [28,29]. It should be emphasized that during childhood, the role of parents is essential for adequate adherence to the GFD. In this context, some studies showed significant discrepancies in the perception of the quality of life between children and parents [30]. Generally, the quality of life of children with CD is often perceived as lower by parents than by their own children [29,31,32]. Therefore, the larger limitations affecting the quality of life of the CD children who followed a GFD for more than 12 months may have been more appreciated by parents than other dimensions, such as dysphoria or health concerns, which may be more introspective.

It is important to highlight that, on average, 47.3% of the participants' total energy intake came from UPFs. In addition, children whose percentage of total energy from UPFs was above 50% showed worse scores for the limitations and inadequate treatment domains of the CD-QOL questionnaire. UPF consumption has a clear negative impact on health, as it is associated with a greater prevalence of overweight, obesity, and cardiometabolic disease and an increased risk of all-cause mortality in adults [17]. The relationships between UPF consumption and diseases can be explain by several mechanisms, including a lower consumption of micronutrients, such vitamins A, B_{12}, C, E, calcium, zinc, fiber, and polyunsaturated fatty acids, and a higher intake of trans fats, sugars, and sodium [15,16]. Furthermore, this eating pattern negatively affects the gut microbiota through the appearance of intestinal dysbiosis, which can trigger a pro-inflammatory immune response and an increase in intestinal permeability [10]. It is known that gut microbiota disturbance [33] plays a key role in the pathogenesis of CD, as colonizing gut bacteria are critical for the normal development of the host defense [34] and for its metabolic and protective function in the host [35]. Various studies have revealed an alteration in the microbiota of celiac patients compared to the healthy controls, observing a reduction in the population of Lactobacillus and Bifidobacterium and an increase in other bacteria, especially Bacteroides, Escherichia coli, and Clostridium leptum [36,37]. Furthermore, a profile of bacterial proteases capable of hydrolyzing gliadin was described in celiac patients that was absent in the healthy controls, confirming a different bacterial proteolytic activity [38]. In this sense, the fact that the CD children in our study had a higher intake of UPFs may have aggravated the pathophysiology of the disease. On the other hand, the fact that CD children consume more UPFs could be due to, but not solely caused by, the characteristics of a poorly completed GFD and, although less likely, a less healthy consumption pattern in this group prior to the onset of the disease due to the relationship of UPFs with the development of intestinal pathologies [10]. In fact, we found that children who consumed less energy from UPFs (i.e., below 50% of their energy) had better redox (lower soluble superoxide dismutase-1 and 15-F2t-isoprostanes) and inflammatory profiles (lower macrophage inflammatory protein-1α) compared with their counterparts [18]. Regarding mental health, previous studies have associated higher UPF consumption with depression [39,40]. Therefore, given the high consumption of this type of food among our participants [18] and the negative repercussions it may have on their health and quality of life, healthcare professionals should perform an adequate follow-up to assess the presence of UPFs in the diets of these patients.

This study has some limitations. Firstly, its cross-sectional design precludes any confirmation of causality. Secondly, the smaller sample sizes for some variables could have prevented the attainment of significance for some associations. Thirdly, the assessment of the participants' quality of life was reported by their parents, which may have differed from the children's own perceptions. However, during childhood, the success of CD treatment and adherence to the GFD depends largely on the parents. Thus, recording their perceptions may be relevant in clinical practice. Fourthly, although it would have been of interest to collect data about the parents' economic income (as it could be related to the children's dietary habits), we included their working status, which could be an indirect measure of their economic position [41,42].

5. Conclusions

The parents of CD children who followed a GFD for 12 months perceived their children as having a lower quality of life, with more limitations related to the disease, especially in the social sphere. In addition, the consumption of UPFs was very high among the celiac patients and was also inversely related to several dimensions of the quality of life, which suggests that it is important to reduce their consumption during disease monitoring. These findings suggest that it is necessary to establish an adequate follow-up of the disease, taking into account the quality of life of the patients once they have started a GFD.

Author Contributions: T.N. and R.M.-M. had full access to all of the data in the study, took responsibility for the integrity of the data and the accuracy of the data analyses, conceptualized and designed the study, interpreted the data, and drafted the initial manuscript. A.L., M.F.-A., M.L.-F., M.d.l.H., J.M. and L.B.-G. collected and interpreted the data. R.M.-M. conceptualized and designed the study. All authors were involved in the drafting of the article and revising it for its important intellectual content. All authors agreed with the order of presentation of the authors. All authors have read and agreed to the published version of the manuscript.

Funding: This research was funded by the FEDER project No. B-AGR-658. It was also partially funded by the grant "Investigation grant program by the Association of Celiacs and Sensitive to Gluten of the Community of Madrid". M.F.-A. was additionally funded by the Spanish Ministry of Education, Culture, and Sports (grant number FPU17/03715). This study is included in the thesis of A.L., enrolled in the doctoral program of Nutrition and Food Sciences at the University of Granada.

Institutional Review Board Statement: The study was conducted in accordance with the Declaration of Helsinki and approved by the Ethics Committee of Clinical Research of the University of Granada, Spain (code: 201202400000697).

Informed Consent Statement: Written informed consent was obtained from all subjects involved in the study.

Data Availability Statement: The data presented in this study are available on request from the corresponding author.

Acknowledgments: The authors thank Nutraceutical Translations for their editing assistance.

Conflicts of Interest: The authors declare no conflict of interest. The funders had no role in the design of the study; in the collection, analyses, or interpretation of data; in the writing of the manuscript; or in the decision to publish the results.

References

1. Ludvigsson, J.F.; Leffler, D.A.; Bai, J.C.; Biagi, F.; Fasano, A.; Green, P.H.R.; Hadjivassiliou, M.; Kaukinen, K.; Kelly, C.P.; Leonard, J.N.; et al. The Oslo definitions for coeliac disease and related terms. *Gut* **2013**, *62*, 43–52. [CrossRef] [PubMed]
2. Al-Toma, A.; Volta, U.; Auricchio, R.; Castillejo, G.; Sanders, D.S.; Cellier, C.; Mulder, C.J.; Lundin, K.E.A. European Society for the Study of Coeliac Disease (ESsCD) guidelinefor coeliac disease and other gluten-related disorders. *United Eur. Gastroenterol. J.* **2019**, *7*, 583. [CrossRef] [PubMed]
3. King, J.A.; Jeong, J.; Underwood, F.E.; Quan, J.; Panaccione, N.; Windsor, J.W.; Coward, S.; Debruyn, J.; Ronksley, P.E.; Shaheen, A.A.; et al. Incidence of Celiac Disease Is Increasing over Time: A Systematic Review and Meta-analysis. *Am. J. Gastroenterol.* **2020**, *115*, 507–525. [CrossRef] [PubMed]

4. Murray, J.A.; Watson, T.; Clearman, B.; Mitros, F. Effect of a gluten-free diet on gastrointestinal symptoms in celiac disease. *Am. J. Clin. Nutr.* **2004**, *79*, 669–673. [CrossRef] [PubMed]
5. Zingone, F.; Siniscalchi, M.; Capone, P.; Tortora, R.; Andreozzi, P.; Capone, E.; Ciacci, C. The quality of sleep in patients with coeliac disease. *Aliment. Pharmacol. Ther.* **2010**, *32*, 1031–1036. [CrossRef]
6. Altobelli, E.; Paduano, R.; Gentile, T.; Caloisi, C.; Marziliano, C.; Necozione, S.; di Orio, F. Health-related quality of life in children and adolescents with celiac disease: Survey of a population from central Italy. *Health Qual. Life Outcomes* **2013**, *11*, 204. [CrossRef]
7. Barrio, J.; Cilleruelo, M.L.; Román, E.; Fernández, C. Health-related quality of life using specific and generic questionnaires in Spanish coeliac children. *Health Qual. Life Outcomes* **2020**, *18*, 250. [CrossRef]
8. Sevinç, E.; Çetin, F.H.; Coşkun, B.D. Psychopathology, quality of life, and related factors in children with celiac disease. *J. Pediatr.* **2017**, *93*, 267–273. [CrossRef]
9. Pynnönen, P.A.; Isometsä, E.T.; Verkasalo, M.A.; Kähkönen, S.A.; Sipilä, I.; Savilahti, E.; Aalberg, V.A. Gluten-free diet may alleviate depressive and behavioural symptoms in adolescents with coeliac disease: A prospective follow-up case-series study. *BMC Psychiatry* **2005**, *5*, 14. [CrossRef]
10. Aguayo-Patrón, S.V.; Calderón de la Barca, A.M. Old Fashioned vs. Ultra-Processed-Based Current Diets: Possible Implication in the Increased Susceptibility to Type 1 Diabetes and Celiac Disease in Childhood. *Foods* **2017**, *6*, 100. [CrossRef]
11. Martínez Steele, E.; Popkin, B.M.; Swinburn, B.; Monteiro, C.A. The share of ultra-processed foods and the overall nutritional quality of diets in the US: Evidence from a nationally representative cross-sectional study. *Popul. Health Metr.* **2017**, *15*, 6. [CrossRef] [PubMed]
12. Moubarac, J.C.; Batal, M.; Louzada, M.L.; Martinez Steele, E.; Monteiro, C.A. Consumption of ultra-processed foods predicts diet quality in Canada. *Appetite* **2017**, *108*, 512–520. [CrossRef] [PubMed]
13. Lustig, R.H. Ultraprocessed Food: Addictive, Toxic, and Ready for Regulation. *Nutrients* **2020**, *12*, 3401. [CrossRef] [PubMed]
14. da Costa Louzada, M.L.; Baraldi, L.G.; Steele, E.M.; Martins, A.P.B.; Canella, D.S.; Moubarac, J.C.; Levy, R.B.; Cannon, G.; Afshin, A.; Imamura, F.; et al. Consumption of ultra-processed foods and obesity in Brazilian adolescents and adults. *Prev. Med.* **2015**, *81*, 9–15. [CrossRef]
15. De Deus Mendonça, R.; Pimenta, A.M.; Gea, A.; De La Fuente-Arrillaga, C.; Martinez-Gonzalez, M.A.; Lopes, A.C.S.; Bes-Rastrollo, M. Ultraprocessed food consumption and risk of overweight and obesity: The University of Navarra Follow-Up (SUN) cohort study. *Am. J. Clin. Nutr.* **2016**, *104*, 1433–1440. [CrossRef]
16. Rauber, F.; da Costa Louzada, M.L.; Steele, E.M.; Millett, C.; Monteiro, C.A.; Levy, R.B. Ultra-Processed Food Consumption and Chronic Non-Communicable Diseases-Related Dietary Nutrient Profile in the UK (2008–2014). *Nutrients* **2018**, *10*, 587. [CrossRef]
17. Lane, M.M.; Davis, J.A.; Beattie, S.; Gómez-Donoso, C.; Loughman, A.; O'Neil, A.; Jacka, F.; Berk, M.; Page, R.; Marx, W.; et al. Ultraprocessed food and chronic noncommunicable diseases: A systematic review and meta-analysis of 43 observational studies. *Obes. Rev.* **2021**, *22*, e13146. [CrossRef]
18. Nestares, T.; Martín-Masot, R.; Flor-Alemany, M.; Bonavita, A.; Maldonado, J.; Aparicio, V.A. Influence of Ultra-Processed Foods Consumption on Redox Status and Inflammatory Signaling in Young Celiac Patients. *Nutrients* **2021**, *13*, 156. [CrossRef]
19. Husby, S.; Koletzko, S.; Korponay-Szabó, I.R.; Mearin, M.L.; Phillips, A.; Shamir, R.; Troncone, R.; Giersiepen, K.; Branski, D.; Catassi, C.; et al. European society for pediatric gastroenterology, hepatology, and nutrition guidelines for the diagnosis of coeliac disease. *J. Pediatr. Gastroenterol. Nutr.* **2012**, *54*, 136–160. [CrossRef]
20. Cole, T.J.; Bellizzi, M.C.; Flegal, K.M.; Dietz, W.H. Establishing a standard definition for child overweight and obesity worldwide: International survey. *BMJ Br. Med. J.* **2000**, *320*, 1240. [CrossRef]
21. Ruiz, M.D.; Artacho, R. *Guía Para Estudios Dietéticos: Álbum Fotográfico de Alimentos*; Universidad de Granada: Granada, Spain, 2011.
22. Moreiras, O.; Carbajal, A.; Cabrera, L. *Ingestas Diarias Recomendadas de Energía y Nutrientes para la Población Española. Tablas de Composición de Alimentos*, 18th ed.; Grupo Anaya, S.A.: Madrid, Spain, 2016.
23. Monteiro, C.A.; Moubarac, J.C.; Cannon, G.; Ng, S.W.; Popkin, B. Ultra-processed products are becoming dominant in the global food system. *Obes. Rev.* **2013**, *14*, 21–28. [CrossRef] [PubMed]
24. Organización Panamericana de la Salud; Organización Mundial de la Salud. *Alimentos y Bebidas Ultraprocesados en América Latina: Tendencias, Efecto Sobre la Obesidad e Implicaciones para las Políticas Públicas*; Organización Panamericana de la Salud: Washington, DC, USA, 2015; p. 76.
25. Dorn, S.D.; Hernandez, L.; Minaya, M.T.; Morris, C.B.; Hu, Y.; Leserman, J.; Lewis, S.; Lee, A.; Bangdiwala, S.I.; Green, P.H.R.; et al. The development and validation of a new coeliac disease quality of life survey (CD-QOL). *Aliment. Pharmacol. Ther.* **2010**, *31*, 666–675. [CrossRef] [PubMed]
26. Zingone, F.; Swift, G.L.; Card, T.R.; Sanders, D.S.; Ludvigsson, J.F.; Bai, J.C. Psychological morbidity of celiac disease: A review of the literature. *United Eur. Gastroenterol. J.* **2015**, *3*, 136–145. [CrossRef] [PubMed]
27. Burger, J.P.W.; de Brouwer, B.; IntHout, J.; Wahab, P.J.; Tummers, M.; Drenth, J.P.H. Systematic review with meta-analysis: Dietary adherence influences normalization of health-related quality of life in coeliac disease. *Clin. Nutr.* **2017**, *36*, 399–406. [CrossRef] [PubMed]
28. Ludvigsson, J.F.; Card, T.; Ciclitira, P.J.; Swift, G.L.; Nasr, I.; Sanders, D.S.; Ciacci, C. Support for patients with celiac disease: A literature review. *United Eur. Gastroenterol. J.* **2015**, *3*, 146–159. [CrossRef]
29. Byström, I.-M.; Hollén, E.; Fälth-Magnusson, K.; Johansson, A. Health-Related Quality of Life in Children and Adolescents with Celiac Disease: From the Perspectives of Children and Parents. *Gastroenterol. Res. Pract.* **2012**, *2012*, 986475. [CrossRef]

30. Vriezinga, S.L.; Farih, N.; van der Meulen-De Jong, A.E.; Putter, H.; Rings, E.H.H.M.; Schaart, M.W.; Schweizer, J.J.; Wessels, M.M.S.; Mearin, M.L. Comparison of Patients' and Doctors' Reports on Health-related Quality of Life in Celiac Disease. *J. Pediatr. Gastroenterol. Nutr.* **2017**, *64*, 737–741. [CrossRef]
31. Torres, J.B.; Roman, E.; Cilleruelo, M.; Marquez, M.; Mearin, M.L.; Fernandez, C. Health-related quality of life in Spanish children with coeliac disease. *J. Pediatr. Gastroenterol. Nutr.* **2016**, *62*, 603–608. [CrossRef]
32. Van Doorn, R.K.; Winkler, L.M.F.; Zwinderman, K.H.; Mearin, M.L.; Koopman, H.M. CDDUX: A disease-specific health-related quality-of-life questionnaire for children with celiac disease. *J. Pediatr. Gastroenterol. Nutr.* **2008**, *47*, 147–152. [CrossRef]
33. Olshan, K.L.; Leonard, M.M.; Serena, G.; Zomorrodi, A.R.; Fasano, A. Gut microbiota in Celiac Disease: Microbes, metabolites, pathways and therapeutics. *Expert Rev. Clin. Immunol.* **2020**, *16*, 1075–1092. [CrossRef]
34. Walker, W.A. The importance of appropriate initial bacterial colonization of the intestine in newborn, child, and adult health. *Pediatr. Res.* **2017**, *82*, 387–395. [CrossRef] [PubMed]
35. Rautava, S.; Luoto, R.; Salminen, S.; Isolauri, E. Microbial contact during pregnancy, intestinal colonization and human disease. *Nat. Rev. Gastroenterol. Hepatol.* **2012**, *9*, 565–576. [CrossRef] [PubMed]
36. Nadal, I.; Donant, E.; Ribes-Koninckx, C.; Calabuig, M.; Sanz, Y. Imbalance in the composition of the duodenal microbiota of children with coeliac disease. *J. Med. Microbiol.* **2007**, *56*, 1669–1674. [CrossRef]
37. Collado, M.C.; Donat, E.; Ribes-Koninckx, C.; Calabuig, M.; Sanz, Y. Imbalances in faecal and duodenal Bifidobacterium species composition in active and non-active coeliac disease. *BMC Microbiol.* **2008**, *8*, 232. [CrossRef]
38. Bernardo, D.; Garrote, J.A.; Nadal, I.; León, A.J.; Calvo, C.; Fernández-Salazar, L.; Blanco-Quirós, A.; Sanz, Y.; Arranz, E. Is it true that coeliacs do not digest gliadin? Degradation pattern of gliadin in coeliac disease small intestinal mucosa. *Gut* **2009**, *58*, 886–887. [CrossRef]
39. Adjibade, M.; Julia, C.; Allès, B.; Touvier, M.; Lemogne, C.; Srour, B.; Hercberg, S.; Galan, P.; Assmann, K.E.; Kesse-Guyot, E. Prospective association between ultra-processed food consumption and incident depressive symptoms in the French NutriNet-Santé cohort. *BMC Med.* **2019**, *17*, 78. [CrossRef]
40. Gómez-Donoso, C.; Sánchez-Villegas, A.; Martínez-González, M.A.; Gea, A.; de Deus Mendonça, R.; Lahortiga-Ramos, F.; Bes-Rastrollo, M. Ultra-processed food consumption and the incidence of depression in a Mediterranean cohort: The SUN Project. *Eur. J. Nutr.* **2020**, *59*, 1093–1103. [CrossRef]
41. Galobardes, B.; Morabia, A.; Bernstein, M.S. Diet and socioeconomic position: Does the use of different indicators matter? *Int. J. Epidemiol.* **2001**, *30*, 334–340. [CrossRef] [PubMed]
42. Marmot, M.; Feeney, A. General explanations for social inequalities in health. *Soc. Inequalities Cancer* **1997**, *138*, 207–228.