Chapter 19

Quality of Life and Psychological Distress in Celiac Disease

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Abstract

Both the quality of life and the psychological status of celiac disease patients have been explored in recent research. This chapter aims to review the reported evidence on the psychological aspects of celiac disease and the patients' perception of the disorder. Nevertheless, studies show controversial and contradictory results. When evaluated prior to diagnosis, patients with a symptomatic clinical presentation had an evident decrease in their quality of life. The gluten-free diet improves such perception. On the other hand, evidence on the quality of life in patients with subclinical disease is not so clear. Depression is the most commonly referred and studied mental disorder. Depression has been reported to be more prevalent and severe in celiac patients than in the general population. The interaction between physiological and environmental factors, seems to be responsible for the disturbance. Anxiety disorders have also been reported, but with less clear results. Currently, it seems accurate to consider them to be forms reactive to diagnosis or to be associated with difficulties in following the diet and its impact on social life. In this sense, the evidence seems to suggest that these could be considered as adjustment disorders with an anxiety state. Regarding the effects of treatment on these symptoms, there is currently no agreement since improvements have been reported in some studies but not in others. Importantly, depression may affect the adherence to treatment, disease evolution and perception of quality of life and, therefore, its presence ought to be investigated upon diagnosis.

1. Introduction

Celiac disease (CD) is an autoimmune chronic T cell-mediated enteropathy, precipitated by gluten ingestion, that appears in genetically predisposed individuals affecting, affecting around 1% of the general population.[1] The gluten-free diet (GFD) is the only treatment that effectively relieves its symptoms, normalizes biochemical changes and the disease's intestinal mucosal damage.[1] Lifelong compliance with the GFD can be challenging for the patients due to its high economic cost, social restrictions and difficulties in complying with it.[2] For these reasons, in recent years, there has been growing interest in evaluating a number of issues such as: whether the disease affects the patients' Quality of Life (QoL), if this is related to clinical presentation characteristics, if the treatment has a positive impact on these parameters or if mood disturbances, such as depression or anxiety, could influence the QoL and compliance with the GFD.[3-6]

Given the evidence of an extremely wide variability range of CD symptoms, recent efforts have sought to clarify and unify clinical criteria.[2] Thus, clinical CD presentations have been classified into: Symptomatic (with intestinal and extraintestinal symptoms, also called classical CD) and subclinical (patients with or without the characteristic signs that occur below the threshold of clinical detection).[2] It is to be expected, as confirmed by research, that clinical differences correlate with psychological aspects and QoL, both before diagnosis and after starting the GFD.[7]

This chapter will explore existing scientific knowledge about the relationship between CD and QoL, psychological distress, depression and anxiety, as well as the implications and consequences entailed by a treatment based on the GFD.

2. Quality of Life

Health Related Quality of Life (HRQoL) expresses health status as perceived by the individual, in relation to the disease itself and the effects that treatments have on the recipient; it is quite clear that this concept focuses on the patient's subjective aspect. HRQoL measurement is a quantitative assessment of the health status and it includes not only physical but also emotional and social aspects. Such measurement has become mandatory in the analysis of the effectiveness of the treatments employed and the evolution of specific conditions, especially in chronic diseases. HRQoL analysis is based on a multidimensional concept, which includes assessment of the patient's psychological well-being, emotional state, physical and social functioning and general health perception.[3-6] Regarding gastrointestinal diseases, the most important aspects include the perception of gastrointestinal symptoms relief and the benefits it may bring to the functional status and general well-being.[4] HRQoL can be measured by a variety of instruments, both general and disease-specific questionnaires. General questionnaires cover a wide spectrum of domains and allow comparison between different diseases and populations, whereas disease-specific questionnaires for each focus on particular aspects of it and its treatment and are more sensitive in detecting small changes in the QoL.[6] Most studies assessing QoL in CD patients used general questionnaires that focus on generic items developed for chronic diseases. The most frequently used are: *Short Form Health Survey* (*SF-36*), the *Psychological General Well-being* (*PGWB*) index, *EuroQuol-5D* questionnaire (*EQ*) and the *Gastrointestinal Quality of Life Index* (*GIQLI*).[3-6] The SF-36 measures functional status and well-being and it includes eight items divided into three categories: physical health status, mental

status, and a combination of both which includes vitality and general health.[4,9,11] GIQLI is a self-administered questionnaire designed to assess QoL in patients with gastrointestinal diseases.[5] EQ is a self-administered questionnaire with a descriptive profile along with a QoL index. It covers five areas: mobility, self-care, daily activities, pain and anxiety-depression.[5,7,9] PGWB is a validated and reliable questionnaire which allows evaluating the patient's distress and mental state.[10] In recent years CD-specific questionnaires have been introduced both for pediatric and adults populations but, unfortunately, evidence for their efficacy is still limited.[3,5,6]

2.1. Quality of Life in Celiac Disease Patients: Importance of Clinical Presentation and Effect of the Gluten-Free Diet

Since the beginning, the investigations focused on the analysis of CD patients' QoL, it was believed that QoL was significantly reduced before diagnosis. Later studies with an adequate clinical characterization, revealed and confirmed the impression that, before diagnosis, patients with active disease and classical gastrointestinal symptoms show a marked decrease in QoL when compared with the general population.[4,7,9] In this context, prospective studies have shown that symptomatic celiac patients submitted QoL diagnostic scores similar to those of patients with chronic disabling disorders such as those cerebrovascular accidents.[7]

A limited number of studies have shown that individuals diagnosed with CD as a consequence of screening in populations at high risk for the disease have a better QoL than patients diagnosed on the basis of symptoms[8,12-15] (Figure 1). It is noteworthy that the vast majority of those surveyed who turned out to have CD, corresponded to the subclinical group. The longitudinal study made by Nachman et al[12], with a four-year follow-up after diagnosis, showed that surveyed patients had QoL scores similar to those of the general population without significant changes from the baseline. A recent study by Rosén et al.[17] evaluated QoL in adolescents diagnosed by screening in a high-risk population. In this study, it was observed that, despite the fact that this population was characterized as subclinical, not all patients saw themselves as healthy and that the CD diagnosis, along with its treatment, represented a benefit to their health. However, a subgroup saw the illness as a stigma that limited their daily lives which, especially in the social field, was more pronounced in the female gender.

In general, these studies suggest that the onset of the GFD implies an improvement in the QoL which, for some authors, produces similar long-term scores to those of the general population.[8] However, other authors suggest that QoL improvement due to the GFD does not come close to the general population's perception.[6,11] A quick assessment of these disparities regarding response to the GFD suggests it could be due to cultural differences between the populations involved; however, the most notable differences seem to lie in the type of research design. Thus, most of the research studies use a crossover design which evaluates different populations both at the time of diagnosis and after treatment; this methodological aspect diminishes the conclusions' value. The few studies which had a prospective and longitudinal design suggest that GFD has a significant impact on the QoL of patients. Moreover, some studies reported a positive GFD impact regarding the QoL, both in its classical and subclinical forms. Thus Ciacci et al.[27] found that 84% of the patients improved their QoL perception after initiating the GFD. Casellas et al.,[5] who evaluated the QoL using the GIQLI and EQ questionnaires before treatment and after the GFD, found that diminished values in both pre-treatment questionnaires improved significantly after GFD and that they were similar to those of the general population. Finally,

Nachman et al.[8] confirmed these observations and showed that the positive impact of the GFD was more significant in the first three months after starting specific treatment (Figure 1). The QoL scores after one year of GFD were comparable to those of the general population, regardless of clinical severity of the diagnosis or the degree GFD compliance (Figure 1). Interestingly, the continuation of this longitudinal study showed a deterioration in the SF-36 items after 4 years of treatment (Figure 2). The most remarkable point regarding this observation is that patients who adhered strictly to the GFD had a similar QoL to that of controls. Conversely, partially compliant patients had a significant deterioration of the QoL (Figure 3).[12] An interesting finding of this study was that patients with less severe symptoms at the time of diagnosis had a decrease in QoL indexes after four years of GFD regardless of the degree of compliance to the latter. The authors postulate that this effect might be due to the burden such a restrictive diet would imply in relation to low disease perception.[12]

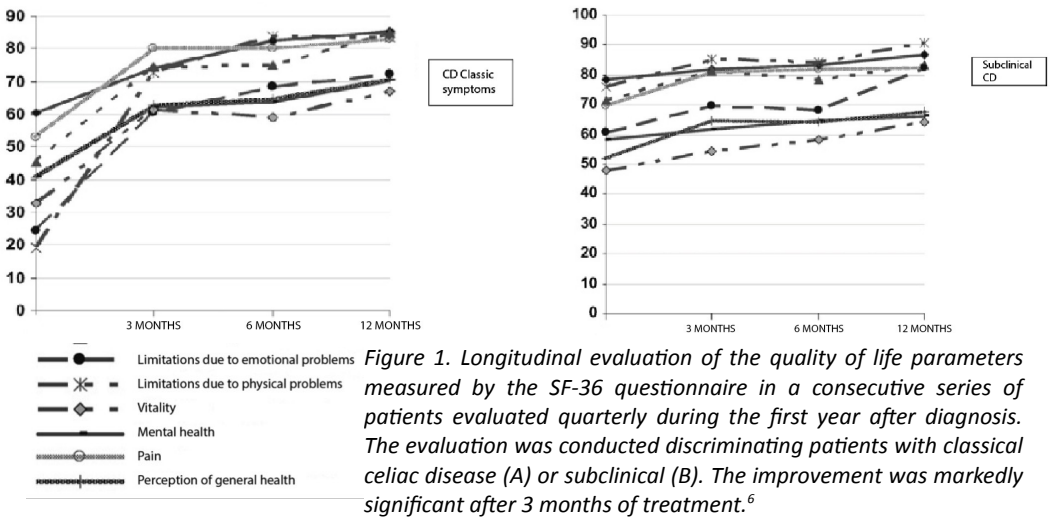

Figure 1. Longitudinal evaluation of the quality of life parameters measured by the SF-36 questionnaire in a consecutive series of patients evaluated quarterly during the first year after diagnosis. The evaluation was conducted discriminating patients with classical celiac disease (A) or subclinical (B). The improvement was markedly significant after 3 months of treatment.[6]

Most observations suggest that female CD patients often have greater QoL impairment than men, both at the time of diagnosis and after treatment, even with strict GFD compliance. These findings are mainly observed in the different mental domains of the questionnaires.[3,5,6,9,11] It has been proposed that this phenomenon may be due to the higher prevalence of anxiety in women.[6] The presence of clinical symptoms and a decrease in the QoL could be related to the existence of a second undetected disorder, often irritable bowel syndrome, pancreatic insufficiency, bacterial overgrowth or microscopic colitis.[6,14]

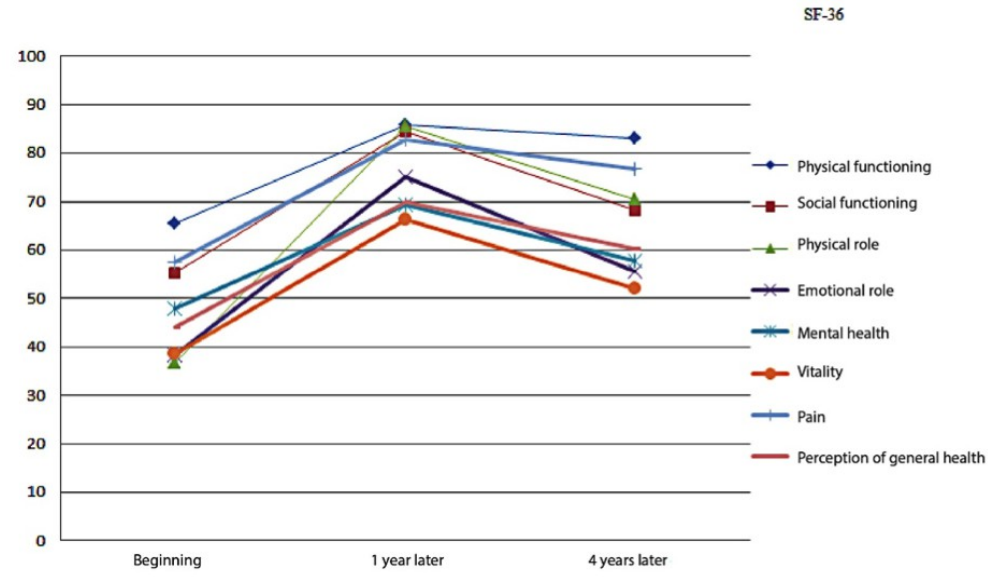

Figure 2. Quality of life reported by SF-36 questionnaires in a general population of celiac disease patients evaluated at the time of diagnosis, at one and at four years after starting treatment. The score increase after one year means an improvement in the evaluated parameters. A deterioration is observed in most parameters after four years.[12]

Summing up this section, patients with CD have a lower QoL than the general population. Evidence suggests that this involvement is important in symptomatic patients, especially those with classic symptoms. By contrast, the few studies on (usually subclinical) patients diagnosed by screening concur on the fact that these patients have no QoL decline. The GFD produces rapid improvement of all QoL aspects in symptomatic CD patients. The response of subclinical patients to treatment would seem to be of little significance.

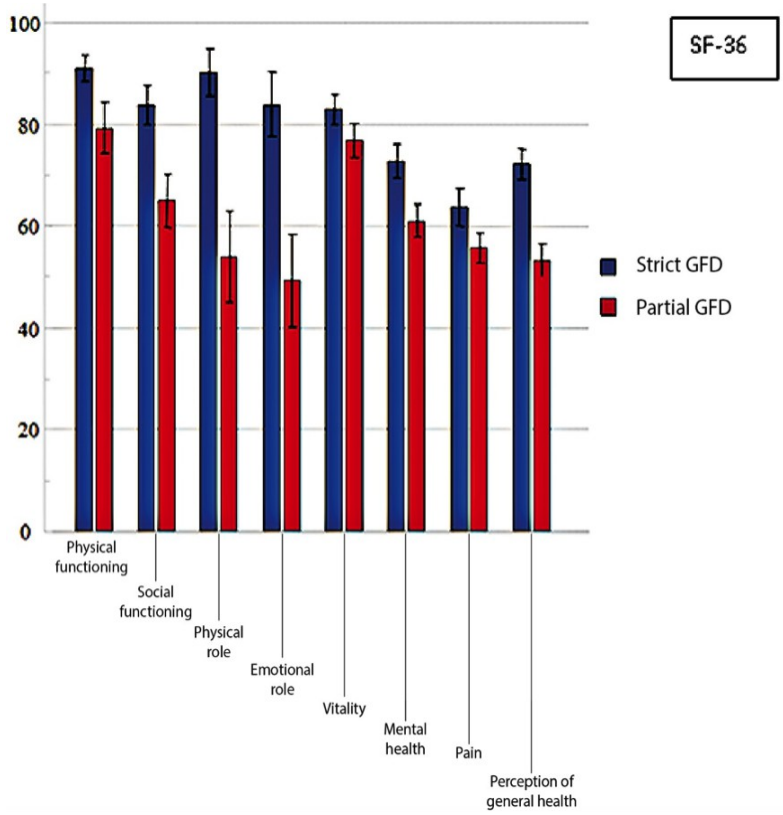

Figure 3. Quality of life after four years of follow-up according to the degree of compliance with the gluten-free diet: Strict (blue bars) or partial (red bars). Patients with strict adherence scores have significantly better QoL than those with partial compliance.[12]

3. Celiac Disease and Psychological Disorders

Addressing the issue of psychological distress in CD is, at first glance, very interesting but often difficult to understand. A multiplicity of studies have focused on its evaluation, especially during the last decade, with dissimilar and even contradictory results. Since the first descriptions of the disease, references were made to psychological symptoms and disorders, albeit in a vague fashion which was not consistent with a specific condition. Thus, for example, these descriptions spoke of a "weariness" which was considered to be psychic in origin, since it which persisted even when the patient had improved clinically.[18] Behavior characterized by "tantrums, irritability and a negative attitude" was described, in 1950, in a group of children who changed dramatically immediately after starting the GFD, while, in adults, a "syndrome of insomnia, depression and headache" was described.[19]

Throughout the disease's short history, celiac patients have been characterized as mentally peculiar, nervous, unstable, depressed and even as schizophrenic.[20,21] By 1970, D. Goldberg[22] performed the first standardized assessment of a series of a group of patients on a GFD and found a high prevalence of depressive traits that showed no relation either with gastrointestinal symptoms or nutritional status. After one-year follow-up, the same author found no schizophrenic patients among those evaluated (a disease that had been previously reported by Dohan[21]) and noted that those individuals who remained sick often had a family history of psychiatric illness. He concluded that signs of depression, common in celiac patients, were possibly related to genetic factors. Subsequently, other authors also found a higher prevalence of psychiatric history prior to CD diagnosis, depression being the most frequently associated psychic disorder.[23] Furthermore, anxiety disorders (diagnostic reactive anxiety state, social phobia and panic disorder) have also been associated with CD but, in this case, without conclusive evidence.

4. Anxiety

While high levels of nonspecific anxiety have been reported in celiac patients, this does not appear to be a stable personality trait, but a state reactive to diagnosis or secondary to symptoms. A study by Addolorato et al.[24] seems to suggest this. These authors assessed anxiety and depression using the *Hamilton State-Trait Anxiety* scale and the *Zung Self-Rating Depression Scale*, respectively. They found that anxiety reversed in the following year. A significantly higher number of patients with panic disorder and depression has also been reported but generally associated with a third very common CD medical condition, autoimmune thyroiditis. Therefore, the authors propose a possible causal association.[25]

Social phobia, another anxiety disorder, has been associated with CD, as well as specific or generalized forms, present both in newly diagnosed patients and in those who were already complying with the GFD.[26] As expected, a significantly higher percentage of associated depression was also observed. This could be considered to be consistent with the findings of C. Ciacci et al.,[27] who described more problems in social life and anxiety related to feeling different from the general population in patients diagnosed after the age of 20, even in cases with good diet compliance. Interestingly, this cross-sectional study of unrelated populations detected no differences between newly diagnosed patients compared with those who were complying with the GFD.[27] Unlike previous evidence, a study performed in Germany suggested an increased risk of a probable anxiety disorder (but not depression) restricted to celiac women complying with GFD when compared to the general population.[28] It is striking, in this study, that the risk was lower among patients who lived alone. Again, we face the question of the weight of social factors and it could be thought that, for some women with celiac disease who adhere to the GFD, the social environment may be experienced more as a burden than as helpful. A 10-year follow-up study by Hallert et al.,[29] which evaluated the burden of the disease in terms of concerns, restrictions and personal balance, showed that women expressed more concern about its impact on relationships with friends and about having to abstain from the "important things" in life. Finally, a recent meta-analysis based on a review of 11 selected studies which evaluated the strength of the association between anxiety and CD, concluded that adults with celiac disease do not differ, in terms of anxiety levels, from the general population or from people with other chronic diseases.[30]

To sum up, anxiety seems to be present in CD patients, not as a characteristic of the disease itself, but possibly as reaction to the diagnosis or the difficulties associated with complying with the diet and its social impact. In this sense, we believe that the diagnosis of an adjustment disorder with an anxiety state, should be considered at least in a group of patients.

5. Depression

Depression is the psychic disorder to which earliest reference is made and the most studied in relation to CD. Here the term is used in its broadest sense without discriminating its different clinical forms, as published studies have used a variety of assessment tools, which do not allow an accurate transposition of their results. In 1982, Hallert and Derefeldt[23] reported similar findings in an area of Sweden with a high prevalence of CD, they reported that 21% of the patients had received psychiatric care prior to diagnosis, depression being the most common finding. In a subsequent study, Hallert and Aström[31] found significantly higher levels in scale 2 of the *Depression Minnesota Multiphasic Personality Inventory-2* compared with a control group of surgical patients. Interestingly, this result did not correlate significantly with abdominal symptoms and these authors described a characteristic depressive mood in patients, different from other medical conditions, such as colitis. This led them to consider depressive psychopathology as a feature of adults with CD, suggesting that this is possibly a consequence of malabsorption, a hypothesis which will be discussed later. In a study by Vaitl and Stouthamer-Geisel, who evaluated a cohort of 182 CD patients using a self-administered questionnaire (*Symptom Check List Revised* (*SCL 90-R*)), observed that a significant proportion of the patients had a history of psychological symptoms for which they had received drug treatment (32%) and/or psychotherapy (14%). These authors concluded that celiac patients had a "psycho-vegetative" state of exhaustion with a distinct depressive component.[32]

Research studies carried out in Italy in 1998 transversely evaluated depression in adult CD patients compared with healthy individuals and patients with persistent chronic hepatitis.[33] Using a modified version of the *Zung Self-Rating Depression Scale,* they concluded that depressive symptoms are characteristic of celiac patients, independently of the time of diagnosis and GFD compliance. Despite these limitations in establishing these new conclusions, these authors identified three main characteristics associated with CD: reactivity, pessimism, asthenia and anhedonia. Also Addolorato et al.[24] found that a large number of patients had depression, and that this was maintained without significant changes after one year with a GFD. The authors proposed that this depression may be related to a reduction in QoL. Recently, two longitudinal and prospective studies by Nachman et al.[8,12] which evaluated QoL and depression at the time of diagnosis and after four years' follow-up, showed high percentages of initial depression, especially in patients with classic symptomatic clinical course (gastrointestinal symptoms). This condition improved dramatically after a year with the GFD, and deteriorated slightly during the four-year evaluation, without reverting to the initial pathological levels (Figure 4). The authors found an inverse relationship between depressive symptoms and adherence to the diet (Figure 5). Similarly, Finnish authors detected an initial improvement in QoL in a group with a GFD after a year of treatment; however, QoL evaluated eight years after diagnosis worsened in relation to the control group. Despite differences in research regarding the populations involved materials, the methodology applied to the investigations and results that preclude comparison between studies, we can say that there is enough consensus in that depression occurs with greater

frequency and severity among celiac patients than in the general population. Additionally, a very large population study in Sweden found a statistically significant association between CD and depression, which seems to leave no room for doubt[34]. Finally, a recent meta-analysis published by Smith and Gerdes[30] came to a similar conclusion reviewing 18 different published studies. These authors concluded that more than 8,000 new negative reports would be required for the association if these results were to be denied. However, there is no agreement in the literature regarding the effects that the GFD has on these symptoms, having reported improvements in some studies[8,12,36,37] but not in others.[24,33]

Summing up, depression is demonstrably associated with CD and its evaluation should be part of the diagnosis. It is important to consider that depression can adversely affect the course of the disease by decreasing the motivation and energy to comply with the diet, having a negative impact on interpersonal relationships including the doctor-patient relationship and inducing a negative evaluation of treatment outcomes by the patient.[51] Depressed people are three times more likely not to comply with treatment than those who are not.[52] Regarding the effects the GFD has on depression, it is still premature to draw conclusions given the differences shown by this research. Surely the assessment of advantages and disadvantages of treatment is one of the future lines of enquiry. Finally, an interesting field arises today regarding absorption-related factors and immune processes, especially inflammatory processes related to the gut-brain connection.[32]

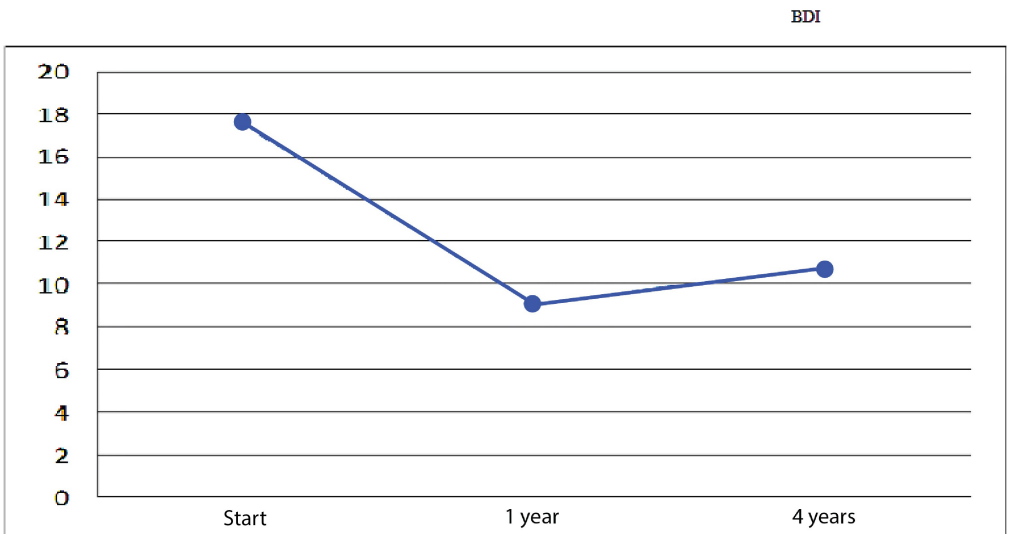

Figure 4. Depression level progression at the time of diagnosis and during long-term monitoring (one to four years) as measured by the Beck Depression Index (BDI) in a series of CD patients.[12]

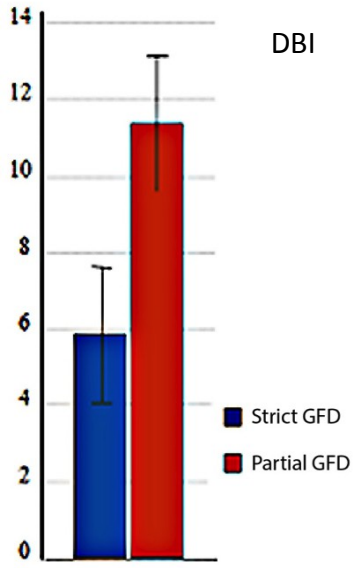

Figure 5. Depression levels four years after diagnosis as measured by the Beck Depression Inventory (DBI) index in a series of celiac disease patients categorized according to the degree of compliance with the gluten-free diet (blue bar: Strict compliance, red bar: Partial compliance).[12]

5.1. Research on the Pathophysiology of Depression

From the pathophysiological point of view, depression is a complex and multifactorial condition generated by several kinds of factors, including, among others: Biological, such as nutritional (linked to malabsorption and its consequences), genetic, immunological and endocrinological.[25,43] In addition, one must consider the psychological and environmental factors since CD is a chronic disease[51] where suffering can be generated by the symptoms and the inconvenience of having to follow a lifelong restrictive diet. Nutrient malabsorption could be the mediating mechanism between CD and depression by interfering with the production of key neurotransmitters for mood regulation, in particular, deficiencies relative to tryptophan malabsorption, necessary for the production of serotonin, a key neurotransmitter for mood regulation.[35] Hallert et al.[36] determined metabolite concentrations of the three major monoamines in cerebrospinal fluid in a short series of patients and found a significant reduction in the levels of 5-hydroxy-indole acetic, homovanillic acid and 3-methoxy-4-hydroxy feniletilenglicol (MOPEG), all of them indicative of a reduction in the central metabolism of the three monoamines (serotonin, dopamine and norepinephrine). Their concentrations, particularly those of MOPEG, inversely correlated with depressive symptoms. In a subsequent study, the same authors explored monoamine concentrations in patients treated with a GFD.[37] This study suggested that the low level of the same could be related to poor intestinal absorption. Monoamine synthesis is regulated, among other dietary components, by vitamin B6, which is generally malabsorbed by celiac patients. The same Scandinavian group followed up celiac patients diagnosed with depression who had not improved after one year despite the GFD having normalized their mucosal intestinal damage.[38] When they were reassessed three years later and after receiving vitamin B6 orally (80 mg/day of pyridoxine), they observed a significant decrease in depressive symptoms. In a multicenter, double-blind study on patients who followed a strict GFD and took daily vitamin B supplementation, normalization of plasma homocysteine levels (marker of B vitamin status) was

demonstrated, which correlated with the improvement of the general welfare and significant decrease in anxiety and depression.[39] Other malabsorption effects can cause symptoms that are confused with and/or overlap with depression. Folic acid deficiency can cause fatigue, apathy, and impaired memory. Iron deficiency, with or without anemia, can cause tiredness and easy fatigue. In this regard, an Italian study more recently assessed the prevalence, characteristics and associations of chronic fatigue and depression.[40] The results showed that fatigue is a feature of CD which improves little with the GFD. These authors suggested that fatigue may have a cognitive and affective origin and that it would tend to decrease in treated patients, while depression would remain or even worsened.

CD is associated with other autoimmune endocrine diseases such as type I diabetes mellitus and Hashimoto's thyroiditis, both with increased risk of depression.[41,42] Carta et al.[25] found a high prevalence of panic and depression disorders in those celiac patients with positive antithyroid antibodies. They suggested that the association with subclinical thyroiditis could represent a significant risk factor for these psychiatric disorders. Garud et al.[43] studied the prevalence of psychiatric and autoimmune disorders in CD, finding that the risk of depression was the same as that of the general population, but that it became higher when associated with DM1, doubling the percentage of patients with clinical depression.

6. Celiac Disease and the Emotional Realm

The psycho-emotional component of CD cannot be dismissed given that psychological distress and social and emotional adaptation to the disease and its treatment surely play an important role. Depression can develop as a result of the discomfort produced by symptoms of the disease, even in the very frequent cases in which the patient doesn't receive an initial diagnosis and wanders from one doctor to another for years, without finding an answer to his or her condition. Again we find some contradictory results, since at least in two studies depression did not correlate with the presence of somatic symptoms.[11,28] However, Nachman et al.[8] while evaluating a cohort of patients at the time of diagnosis using the Beck Depression Inventory (BDI), found a high prevalence of moderate and/or severe depression in patients with symptomatic classical clinical presentation, but with values equal to the general population in subclinical cases. In a recent epidemiological study conducted in Canada, the annual prevalence of major depressive disorders in people with one or more diseases was 9.2% compared with 4.0% in those who reported no other condition.[44] In this study, major depression in people with bowel disorders, Crohn's disease and colitis was of 16.4%, findings similar to those of other investigations.[45,46] All chronic diseases have a strong impact on the QoL. One of the major changes, perhaps generating further deterioration, is the emotional aspect, since the person is necessarily forced to undergo a rapid adaptation process, which passes through different stages, which evoke a range of usually negative emotions (fear, anger, anxiety). In the case of CD, it may appear that the balance of the necessary dietary changes with a view to their intended is highly positive. In this sense, it should not be very difficult to accept the disease and certainly benefits, this happens often. However, adaptation to GFD is more difficult than it seems upon first impression. Patients must make permanent changes to important aspects of their life and regarding self-control, for which they need knowledge, skills and discipline. Considering these difficulties, it is not surprising that a significant number of patients develop psychosocial problems. Linking all these factors, an Italian study evaluated the impact of a chronic disease in relation to CD's psychiatric symptoms, the

degree of acceptance of the disease and the impact that the diet has on QoL.[4] The results showed significantly high anxiety levels and depression in the celiac group and in the diabetic group compared with healthy controls. Furthermore, the duration of the gluten restriction correlated with significantly depression higher levels in newly diagnosed patients. The authors concluded that frequent affective disorders in celiac patients are linked to the fact that it is a chronic disease and to difficulties in adjusting to the diet, and should not be considered disease traits in themselves.

Diet restrictions have a bigger influence on the style of life of celiac patients than what it was previously thought since they strongly interfere in daily activities and social life. A survey of celiac patients (74% women) showed several areas where maintaining a GFD has a negative impact in situations such as eating out with the family, travelling and at work.[48] An interesting Swedish study dealt with situations which often lead to confusion and discomfort in relation to the disease causing conflicts (dilemmas) to celiac people with a GFD.[49] The results indicated that they affect different areas: the emotional area, interpersonal relationships and celiac patient's daily activities in different settings: at work, shopping, travelling, and eating out and at home. The predominant feelings were: isolation, shame, fear of gluten contamination and concern over being troublesome. In interpersonal relationships, situations like being forgotten or neglected, not wanting to draw attention because of the disease and to avoid talking about the subject or lowering their guard so as to avoid being exposed. Finally, daily life complications are related to the lesser availability of gluten-free products, increased effort and to being constantly vigilant and alert. However, despite the above, many patients with chronic diseases do not show high levels of distress, which raises the question of which may be the protective factors. Many studies have shown the importance of considering the individual characteristics and coping skills of patients as central factors. The way in which a patient responds to problems can be become a favorable or negative point for our physical and mental wellbeing. In this regard, the presence of a specific celiac psychological profile has been suggested.[50] Its main characteristics would be high irritability accompanied by high psychophysiological reactivity and a kind of conformity that reflects both the difficulty in expressing feelings as much as the desire to have a good image in front of others. The authors proposed that this increased psychophysiological reactivity could be related to the worry and the weight of shouldering a chronic disease, as well as with hyper vigilance in relation to food. The trend towards a conforming behavior may be related to avoidance of situations with greater exposure consistent with a lifestyle limited by the presence of a chronic disease.

7. Conclusions and Recommendations

In recent years, the QoL concept in relation to CD has become relevant. Classic CD patients prior to diagnosis showed a low QoL, which experience a significant improvement by the GFD. In contrast, the situation in patients with subclinical CD is not as clear. Depression is more prevalent and more severe in celiac patients than in the general population. We do not know if there is a major etiopathogenic factor that accounts for it; however, it is more appropriate to think in the synergy of several factors that possibly interact in varying proportions. On the other hand, there is no such certainty regarding anxiety disorders. In any case, it is necessary to take into account the need to assess the presence of both disorders at the time of diagnosis, especially depression. This recommendation is related to the proven association that this mental disorder has on the

development, adherence and response to treatments, as has been observed in various chronic diseases. Its evaluation during primary care consultations can be done by means of simple questions and from there it can be decided whether the case is suitable for psychiatric or psychological referral.

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