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Original Research

The evolutionary profile of celiac disease via the compliance to the gluten-free diet in the western Algerian region

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Abstract

Background and aims: To assess the compliance to the gluten-free diet (GFD) of Algerian patients with celiac disease (CD) and to study the impact of long-term GFD on anthropometric, serological, and histological parameters of these patients. **Material and method:** We conducted a retrospective study on 111 cases of CD patients followed up, from pediatric age until now, at the pediatrics department of the ORAN University Hospital Centre for many years. Two groups were made according to their adherence to the gluten-free diet. **Results:** The clinical presentation of the disease was typical (84.7%) and atypical (15.3%). Two groups were selected group A and B for non-compliant diets (39.6%) and compliant diets (60.4%), respectively. There was a significant difference between the current age and the two groups of adherence (p=0.008) and with body mass index (BMI) ($p<10^{-3}$). However, we noticed an excellent significant difference between a serology under diet and two groups (p=0.001) also with the grade of histology ($p<10^{-3}$). Moreover, a significant reduction of IgA and IgG anti-t-TG in group B (p=0.001). **Conclusions:** CD in Algeria is still characterized by heterogeneous clinical symptoms and good compliance to the GFD is a sign of the path to recovery.

Keywords: celiac disease, gluten free diet, compliance, IgA and IgG anti transglutaminase.

Background and aims

Celiac disease (CD) is a chronic disorder, autoimmune enteropathy, with an immunoreaction to gluten in genetically susceptible subjects [1]. It poses a major public health problem, and the prevalence has been approximately underestimated (1–3%) in children [2, 3]. However, the prevalence is exceptional among Sahrawi children in Algeria, it is 56/1000 [4]. The incidence of the disease has therefore increased significantly over the last few decades [5, 6].

The presentation of the disease is heterogeneous with symptomatic, asymptomatic, and latent forms. The symptomatology of the disease of classic form is the most typical and are defined by the gastrointestinal manifestations (GT), but also, can have extra-intestinal manifestations [5, 7, 8]. The current diagnostic strategy for celiac disease is based on clinical suspicion and confirmed by serological, histological tests [9], although the screening and diagnosis of CD are relatively well-established [10].

The therapeutic management of CD is based on dietetics, and the gluten exclusion diet remains the only effective treatment. For this reason, strict and permanent adherence to the diet is a sign of the path to recovery by reducing complications and improving the state of health [11]. The limitations of the gluten-free diet (GFD) compliance may affect the quality of life (QoL) of children [12], that's why the diet remains difficult to maintain in the long term in certain social situations. Knowing factors that affect compliance, would help to improve patients' ability to maintain a strict GFD [13]. Through this study, we aimed to evaluate the compliance to the gluten-free diet (GFD) of Algerian patients with celiac disease (CD) and to study the impact of long-term GFD on anthropometric, serological, and histological parameters of those patients.

Material and method

Study design and patients

We conducted a cross-sectional, observational study of 111 cases of CD diagnosed at pediatric age and followed-up until now at the level of pediatric ward C, clinic A, Cabral of the ORAN University Hospital Center in north–western Algeria. Two groups were made according to their adherence to the GFD: Group A (Non-compliant) and group B (Compliant). Data were collected from the files of CD patients and included the following inclusion criteria: Subjects with celiac disease with the presence of serological and histological evidence diagnosed at pediatric age and who have benefited from care and follow-up in the pediatrics department from the time of diagnosis to the present day. The confidentiality of data was respected. All celiac cases without histological and serological evidence and loss of follow-up have been excluded.

Statistical analysis

The processing and analysis of the statistical data in our sample were carried out via SPSS 22.0 (Statistical Package for the Social Sciences, IBM Corporation; Chicago, IL. August 2013) and was presented in rates and cross-tabulations as well as box plots. Results were expressed as frequencies, means, and standard deviation. The reference values for the comparison between the two groups were made using the 95% confidence interval.

We used the Chi-square test to compare the adherence to the GFD of groups A and B. Correlation between the adherence to the GFD of both groups and the serological, histological, and anthropometric parameters (age, body mass index and hemoglobin) as well as the sensitivity of the autoantibodies were made using the Student t-test. The criterion of statistical significance was $p<0.05$.

Results

In our series, there was a frequency of (51.4%) females and (48.6%) males with a sex ratio of 1.05 (F/M). The average age was at 22.06±4.650 and the most affected age group was [20–29] years with a rate of (57.7%). The average age at diagnosis was 5.86±4.538 years (Table 1).

The mean body mass index in our sample was at 15.17±3.433 kg/m^2 and 80.2% of patients were malnourished [<16.5]. The comorbidity of celiac disease mainly noted in our patients was dysthyroidism at 13.5% and anemia at 10.8%. The symptomatology of the disease was defined by a classic and typical clinical presentation in 84.7% of celiac patients; mainly associated with digestive disorders such as chronic diarrhea (72.1%), abdominal bloating (40.5%), abdominal pain (37.8%), and vomiting (36.9%). Atypical clinical presentation characterized by extra digestive manifestations only occurred in 15.3% of cases, with weight loss (45.9%), failure to thrive (53.2%), and anemia in 32.4% of celiac patients (Table 1).

The gluten-free diet (GFD) has been prescribed to all patients. Thus, CD patients were classified into two groups according to their adherence to the GFD: group A, non-compliant (44 patients, 39.6%), and group B, compliant (67 patients, 60.4%).

No significant differences were found between the age at diagnosis and the age at onset of the disease, as well as between the body mass

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Table 1: Characteristics of 111 patients with celiac disease enrolled in the study.

Characteristics of the population	Number (%)
Gender	
Female	57 (51.4%)
Male	54 (48.6%)
Age range	
(16–19)	39 (35.1%)
(20–29)	64 (57.7%)
(30–39)	08 (7.2%)
BMI slice	
(<16.5)	89 (80.2%)
(16.5–18.5)	14 (12.6%)
(18.5–25)	05 (4.5%)
(25–30)	01 (0.9%)
(30–35)	02 (1.8%)
Family history of celiac disease	19 (17.1%)
Symptomatology	
Typical	94 (84.7%)
Digestive disorders	
Chronic diarrhea	80 (72.1%)
Abdominal Bloating	45 (40.5%)
Abdominal pain	42 (37.8 %)
Vomiting	41 (36.9%)
Atypical	
Extra-digestive events	17 (15.3%)
Weight loss	51 (45.9 %)
Failure to thrive	59 (53.2%)
Anemia	36 (32.4%)
Comorbidity	
Anemia	12 (10.8%)
Asthma	06 (5.4%)
Type 1 diabetes	06 (5.4%)
Dysthyroidism	15 (13.5%)
Helicobacter pylori gastritis	03 (2.7%)
Osteopenia	07 (6.3%)

Values are given as number (%). BMI: body mass index.

index (BMI) value at the time of diagnosis and after 2 years on the diet. Likewise, there were no significant differences in terms of hemoglobin levels at the time of diagnosis in both groups (p=0.06).

On the other hand, there was evidence for a significance between the current age and the two adherence groups, with a mean of (21.52±3.81 years vs. 22.89±5.64 years, p=0.008). Compliancy to GFD also induced a substantial and significant improvement in the health status of the patients by the increase of BMI after 2 years of diet (16.51±4.05 (kg/m^2) and also at the last consultation (21.01±3.28 kg/m^2 (B) vs. 18.63±3.22 kg/m^2 (A)) p<10^{-3}. The hemoglobin value in all patients at diagnosis was estimated at a mean of (6.01±4.39 g/dl). However, an excellent improvement in hemoglobin levels was noted in the compliant group (11.88±0.76 g/dl (B) vs. 11.55±1.13 g/dl (A), p<10^{-3}) (Table 2). Two serological test results were used (serology at diagnosis and regimen serology). No significant difference was noted on serological data at the time of the diagnostic p=0.13. However, the serological test under diet was positive in 43.18% of cases for non-compliant group (A) and in only 14.93% for the compliant group (B) with an excellent significant difference p=0.001.

According to the degree of severity of the lesion of the intestinal mucous membrane, the histological examination after diet, showed that 61.26% of all patients were at grade 3 or: ((27.27% (A) vs. 83.58% (B)), grade 4 was noted in (23.42%): (43.18% (A) vs. 10.45% (B)); and grade 5 in 15.31% of all patients: (29.55% vs. 5.97%) for the patients belong to groups A and B, respectively with an excellent significant difference p<10^{-3}.

Table 3 shows the adherence of the gluten-free diet via serological tests and the severity of intestinal mucosal lesion.

The determination of autoantibodies was done by the Elisa method from the patient's serum, the results (≥20 U/ml) were considered positive. We found a substantial and significant reduction in IgA and IgG anti-tTG isotype antibodies (anti-transglutaminase) (p=0.001) in the compliant group compared to the noncompliant group with a reduction of 09 U/ml for group (B) and 10 U/ml for group (A) (Figures 1 A and B).

Discussion

CD in our study was characterized by a predominance of the female sex with a sex ratio

Table 2: Features of patients' compliance with the gluten-free diet: comparison based on anthropometric parameters.

Characteristics	All patients n=111 (CI 95%)	Non-compliant[a] n= 44 (CI 95%)	Compliant[b] n= 67 (CI 95%)	p-Value*
Age (years)				
Age at diagnostic	5.86±4.53 (5.01–6.71)	6.01±4.39 (4.68–7.35)	5.76±4.66 (4.62–6.90)	0.42
Age of onset of symptomatology	3.09±3.48 (2.43–3.74)	3.36±3.85 (2.19–4.53)	2.90±3.24 (2.11–3.69)	0.22
Current age	22.06±4.65 (21.19–22.94)	22.89±5.64 (21.17–24.60)	21.52 ±3.81 (20.59–22.45)	0.008*
BMI (Kg/m^2)				
During the diagnosis	15.17±3.43 (14.52–15.81)	15.27±4.23 (13.98–16.56)	15.10±2.81 (14.41–15.79)	0.434
After 2 years of the GFD	16.39±3.76 (15.68–17.10)	16.20±3.31 (15.19–17.20)	16.51±4.05 (15.52–17.50)	0.99
Current+	20.06±3.44 (19.42–20.71)	18.63±3.22 (17.65–19.61)	21.01±3.28 (20.20–21.81)	$< 10^{-3*}$
HB (g/dl)				
During the diagnosis	6.01±4.39 (–1.503–2.003)	11.32±1.45 (10.88–11.76)	10.42±1.81 (9.97–10.86)	0.06
After gluten free diet	6.01±4.39 (–1.503–2.003)	11.55±1.13 (11.20–11.89)	11.88±0.76 (11.69–12.07)	$< 10^{-3*}$

Values presented as mean ± standard deviation. BMI: body mass index, HB: hemoglobin, CI: confidence interval. [a]Patients sometimes ate gluten-containing food;[b]Patients were not aware of taking any food containing gluten; *Significant p-value at (p<0.05).

Table 3: Serological characteristics and histological parameters assessed at diagnosis and on a diet by patients' compliance with the gluten-free diet.

Characteristics	All patients n=111	Non-compliant[a] n=44	Compliant [b] n=67	p-Value*
Serology during diagnosis, n (%)				
Positive	97 (87.40%)	41 (93.20%)	56 (83.60%)	0.13
IgA-atTG assay (U/ml)				
Positive	42 (37.84%)	15 (34.09%)	27 (40.30%)	0.52
IgG-atTG assay (U/ml)				
Positive	18 (16.22%)	05 (11.36%)	13 (19.40%)	0.68
IgA-AGA assay (U/ml)				
Positive	61(54.95%)	24 (54.55%)	37 (55.22%)	0.23
IgA-EmA assay (U/ml)				
Positive	17 (15.32%)	07 (15.91%)	10 (14.93%)	0.26
Serology on a gluten-free diet, n (%)				
Positive	29 (26.13%)	19 (43.18%)	10 (14.93%)	0.001*
Histology (Marsh classification), n (%)				
Marsh 3	68 (61.26%)	12 (27.27%)	56 (83.58%)	$<10^{-3*}$
Marsh 4	26 (23.42%)	19 (43.18 %)	7 (10.45%)	
Marsh 5	17 (15.31%)	13 (29.55%)	4 (5.97%)	

Values are given as number (%). tTG IgA and IgG: IgA and IgG type anti-transglutaminase antibodies; IgA AGA: IgA type antigliadin antibodies; EmA-IgA: IgA type endomysial antibodies; *Significant p value at (p<0.05).

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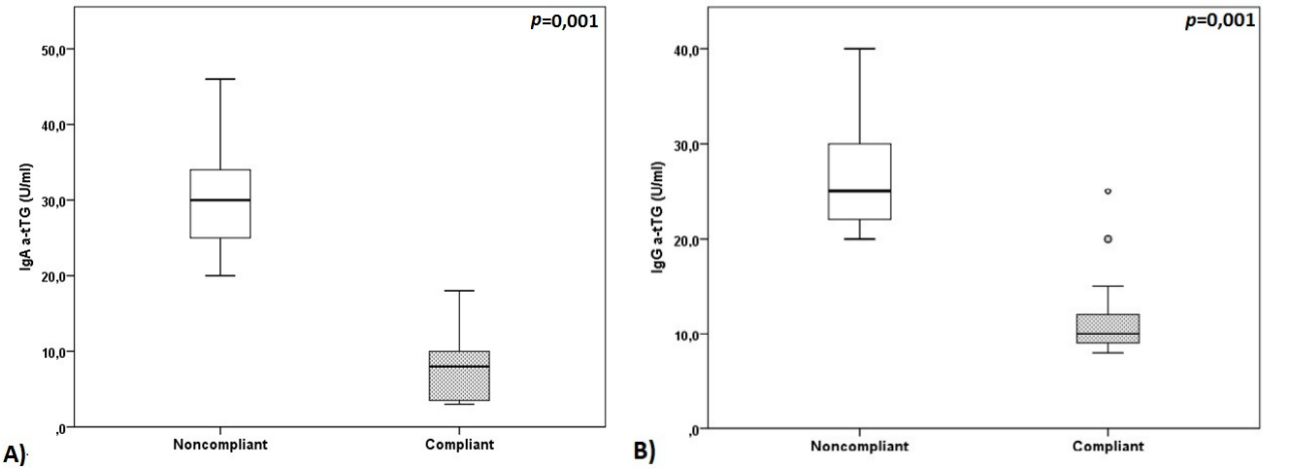

Figure 1: Anti-transglutaminase assay (IgA, IgG) under diet in both groups.

of 1.05. This predominance was also suggested by other studies [14]. In our study, the mean age of onset of the disease was at 3.09±3.48 years and the mean age of diagnostic was at 05.86±4.538 years which agrees with the results of some Algerian studies [15, 16].

The diagnosis of CD is the result of a multi-disciplinary investigation taking into account the clinical data and the severity of the lesions of the intestinal mucosa, the serology as well as the initiation of the GFD [9] which was confirmed by our study.

The classic symptomatology of CD associating chronic diarrhea, abdominal bloating, abdominal pain, and vomiting occurred in (72.1%), (40.5%), (37.8%) and (36.9%) of celiac patients; respectively, it was a typical clinical presentation (84.7%). Our results were similar to several studies [15, 17] from which they suggested that chronic diarrhea is the main symptom characterized by CD in children. Also, atypical symptoms (15.3%) can correspond to extra digestive manifestations such as weight loss (45.9%), failure to thrive (53.2%), and anemia (32.4%). Our results with literature data [8, 15] confirm that celiac disease manifests itself via digestive and/or extra-digestive manifestations in children and adolescents.

The comorbidity of CD has been revealed in our patients with anemia as the main complication associated with CD in relation to the nutritional status and hematological diseases, this was confirmed by [18] findings. Nevertheless, the association of CD with autoimmune diseases has been described in our results, mainly dysthyroidism [19] and type 1 diabetes as reported in the literature [20, 21].

In our series, dietary compliance was evaluated in two groups: non-compliant with the GFD (39.6%) and compliant (60.4%). Our results were confirmed by several studies, which reported that the rate of compliance with a GFD varies between 45% and 90% in CD patients of different ethnicities [22].

This compliance was reported via anthropometric parameters (table 2): a significant correlation between the two groups and the current age (22.89±5.64.vs21.52 ±3.81, p=0.008), this confirms that GFD compliance can be influenced by age at diagnosis [22]. This compliance to GFD induces a substantial and significant improvement in the health status of the patients by the increase of BMI after 2 years of diet (16.51±4.05 kg/m^2) and also the current BMI (21.01±3.28 kg/m^2) ($p<10^{-3}$); and hemoglobin level (11.88±0.76 g/dl) ($p<10^{-3}$) in patients who completed the diet well. Our results are consistent with those of [23] but this compliance remains difficult to maintain in the long term if we take into consideration the quality of life of the patients [24].

Similarly, serological tests related to celiac disease are commonly used as markers for the detection of the disease and are even recommended for screening [25]. Indeed, the serological tests mainly (IgA and IgG a-tTG, IgA EmA, IgA AGA) have an excellent predictive value to confirm the diagnosis [24, 26].

This study confirms that the intestinal biopsy is still considered as the reference test for the diagnosis, a predominance of grade 3 villous atrophy according to the Marsh classification was observed in (61.26%) of our patients, confirming the results of [27] showing that 43.18% of the CD patients not compliant the diet having villous atrophy of grade 4. Excellent significance level ($p<10^{-3}$) between the grade of the atrophy and the two groups of compliance of diet was observed. Our results suggest that histological recovery depends on good compliance with the GFD [28].

The treatment by a gluten-free diet has led to significant qualitative and quantitative changes in the antibodies linked to the disease [22]. These antibodies are the anti-transglutaminase isotype IgA and IgG because of their specificity and sensitivity [22]. Our results confirm a significant reduction (p=0.001) in the rate of anti-transglutaminase isotype IgA and IgG autoantibodies positivity in group B.

Conclusions

This study confirmed that CD in Algeria is still characterized by a typical clinical presentation and that changes and/or reduction of antibody levels are influenced by the degree of adherence to the diet by patients despite the fact that this diet is difficult to maintain in the long term in some social situations. In a long-term perspective study in different regions of our country, it is necessary to know more about the objective measures to evaluate the adherence to the diet in order to maintain a better response to the treatment.

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Conflict of interest

The authors declare no conflict of interest.

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