CHARACTERISTICS OF ADULT CELIAC DISEASE IN EASTERN ALGERIA

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Summary

The objective of this study was to determine the clinical picture of adult celiac disease in the population of eastern Algeria. We conducted a retrospective study on a sample of 156 patients in Internal Medicine service, Hepato-Gastroenterology Service, Endoscopy Service in the University Hospital BENBADIS - Constantine and the Military Regional University Hospital - Constantine. Our results have shown that, in this population, celiac disease can be manifested by a number of signs and related pathologies. A variety of digestive symptoms were reported, primarily chronic diarrhea (81.4%), abdominal pain (57.1%), anorexia (42.9%) and vomiting (48%). Extra-digestive symptoms manifested mainly as weight loss (90.4%), pallorous of skin and mucosa (84%), asthenia (60,3%), edema of the lower limbs (46.8%) and dehydration sings (37.8%). In addition, we noted biological disorders, the most common being hypocalcemia (77.4%) and hypoalbuminemia (57.7%), and a series associated pathologies namely: anemia (67.9%) and digestive diseases (38.46%). CD in adults in our population may express a variety of digestive and extra-digestive symptoms in addition to a number of associated pathologies.

Keywords: adult coeliac disease, symptoms, associated conditions, Eastern Algeria

Introduction

In genetically predisposed subjects, celiac disease is a chronic immunological disease manifested as enteropathy affecting the small intestine, triggered by the ingestion of gluten [1].

Throughout the world, celiac disease is widespread. Its prevalence among population is one in 100 to one in 300 [2]. It was significantly lower 20 years ago [3]. There are far more undiagnosed cases (below the waterline) of CD epidemiology with iceberg features than diagnosed cases (above the waterline) [4].

The substantial increase in the number of patients diagnosed with celiac disease corresponds with the recognition of a remarkably

large spectrum of clinical symptoms of celiac disease [1, 5, 6], in addition to a true rise in incidence and the development of reliable screening tests [7].

Recognition of broad clinical heterogeneity in the condition, ranging from patients with classical clinical presentations to patients with clinical symptoms considered as atypical or non-classical, is one of several explanations for the increased prevalence of celiac disease. Furthermore, patients may be monosymptomatic or oligosymptomatic [8]. There is a very complex clinical representation of CD, and there are many diseases in which mucosal changes are seen identical to those of CD. The variety of symptoms of this condition is a problem for health practitioners who do not know about celiac disease [7].

The present study aimed to identify the clinical picture, associated conditions and the peculiarities of this disease in our population. We report the results of a retrospective study in the region of eastern Algeria.

Material and Methods

We performed a retrospective study in Internal Medicine Service, Hepato-Gastroenterology Service, Endoscopy Service in the University Hospital BENBADIS – Constantine and The Military Regional University Hospital - Constantine, located in eastern of Algeria. This study was based on the data of 156 patients who were consecutively diagnosed with celiac disease between 2004 and 2014. Data collection was carried out using a data collection card. We

applied, as criteria for inclusion of individuals with celiac disease, of both sexes and aged of 18 years and older. Exclusion criteria were, respectively, absence of celiac disease and subjects less than 18 years old.

SPSS version 20 for Windows was used for descriptive statistics. Results were calculated as frequencies (%), means and standard deviations (SD).

Results

The sample included 59 % females. The results revealed a female to male ratio of 1.4:1 (92 females and 64 males). The mean age of the patients was 34.96 ± 14.49 years (range 18-84), with an average value of body mass index of 18.34 ± 2.88 kg/m². Of the patients studied, 61.1% were underweight and 4.1% were overweight. The median age of the patients at diagnosis was 22.33 ± 18.41 years (range 18-84 years). The disease duration of the majority of patients (40%) was between 5 and 10 years. In 16.7% of patients, we noted the presence of similar cases in the family.

We sought in this study all visceral, clinical or morphological manifestations and any pathology associated with celiac disease. Clinical pictures found digestive symptoms, extradigestive symptoms alone or in association with other diseases. In our series of patients, we did not find asymptomatic forms. The most frequent gastrointestinal symptoms were chronic diarrhea (81.4%), abdominal pain (57.1%), anorexia (42.9%), and vomiting (48%) (Figure 1).
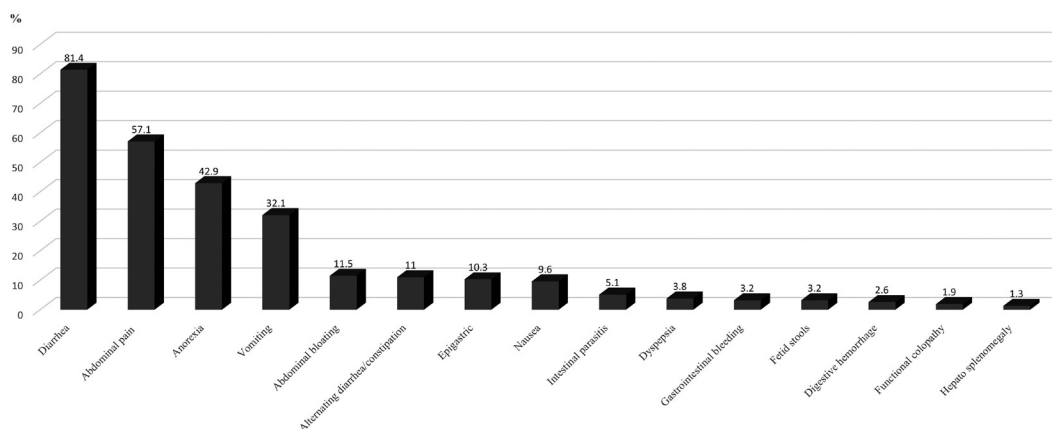

Figure 1. Distribution of gastrointestinal symptoms

Extra-intestinal symptoms were mainly represented by weight loss, pallid skin and mucosae, and asthenia of 90.4%, 84% and 60.3%, respectively. Another series of extra-intestinal symptoms included edema of the lower limbs (46.8%) and dehydration signs (37.8%) (Figure 2).

Our series is marked by the presence of certain conditions associated with digestive or extra-digestive symptoms, represented mainly by anemia and digestive diseases, amounting to

67.9% and 38.46%, respectively. Mouth ulcers were reported in 17.3% and type 1 diabetes – in 16.7% of the patients. The other conditions, associated with celiac disease in this study are presented in Figure. 3.

Among the digestive's diseases, we identified three diseases with the highest percentages: Crohn's disease (6.4%), Wilson's disease (5.1%) and peptic esophagitis (5.1%) (Figure 4).

Regarding neurological diseases, the most common was chronic migraine (5.1%), and 1.9%
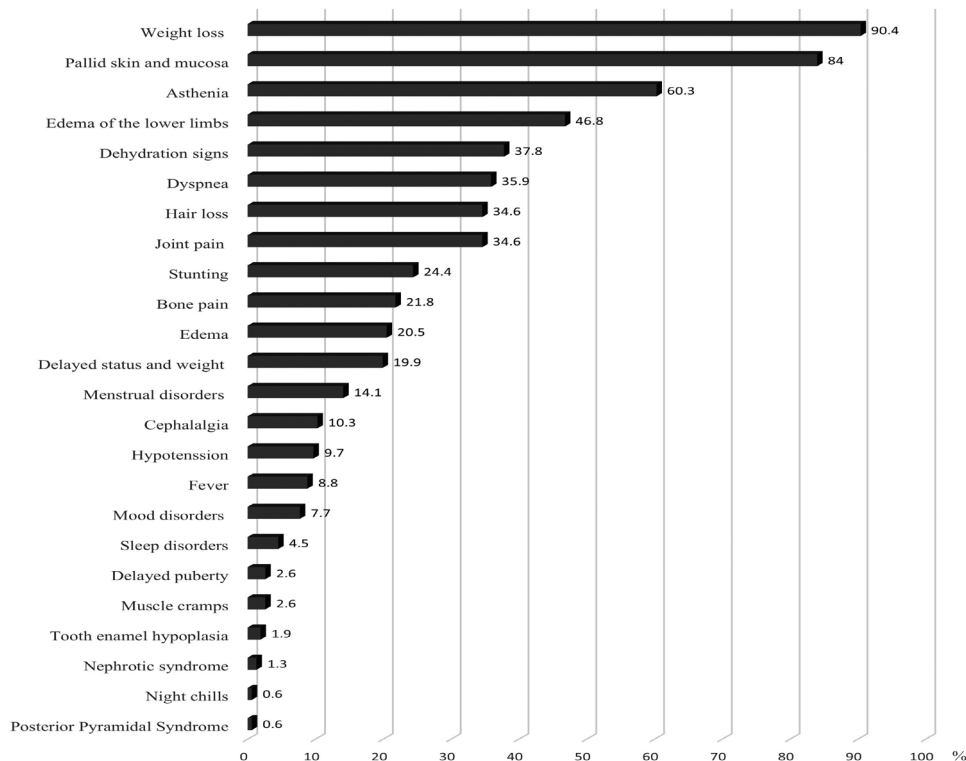

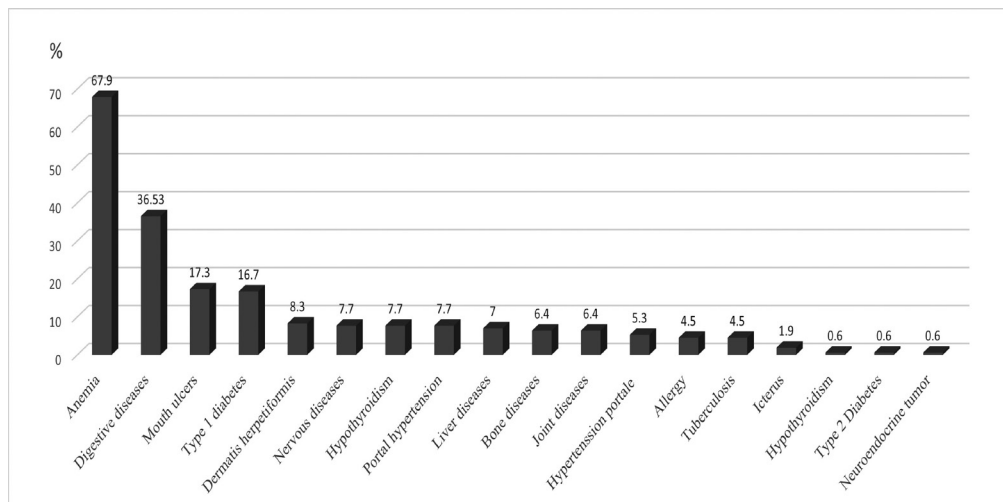**Figure 2.** Distribution of extra-digestive symptoms

Figure 3. Distribution of associated conditions.

of patients reported experiencing depression. Low-frequency of other neurological diseases was also observed, such as cerebrovascular accident, Alzheimer, meningitis and epilepsy (Figure. 5).

Perturbation of biochemical markers was found, mainly represented by hypocalcemia (77.4%), hypoalbuminemia (57.7%), and hypokalemia (42.9%) (Figure. 6).

In this sample of patients, we found that anti-tissue transglutaminase and antigliadin antibody tests presented the highest positive value for untreated celiac disease (Figure 7).

Tests for serum anti-transglutaminase antibodies were requested 117 times, and found positive in 82.9%.

Testing for anti-endomysium IgA antibodies was requested in 111 subjects, 74.8% of which were positive.

Assays of serum anti-gliadin IgA antibodies were requested in 135 patients, and was positive in 77.0%.

Anti-reticulin antibodies were requested only in 59 patients and 76.3% were positive.

In our study, 130 patients had small bowel biopsy. The results demonstrated the diagnosis of CD was correct in 100% of these patients. For histological analysis, 4 grades of the disease were established. The majority of patients in the study had grade 5 of celiac disease (56.2%), followed by those with grade 4 and grade 3 with the percentages of 15.4% and 27.7% respectively. There was only one case with the first grade of the disease.

As shown in the Table 1 below, we noted cases of biopsies indicative of celiac disease with a grade of 3 to 5 of villous atrophy in patients with negative serological tests.
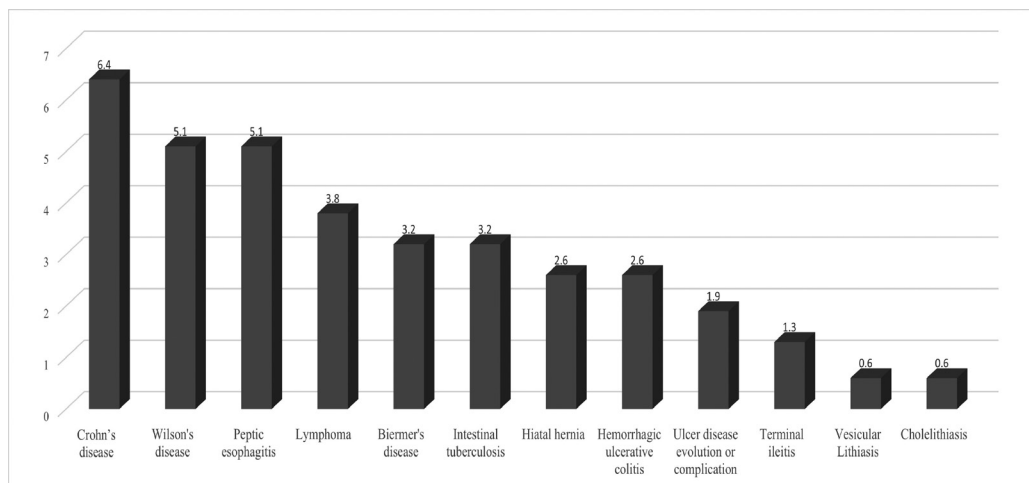

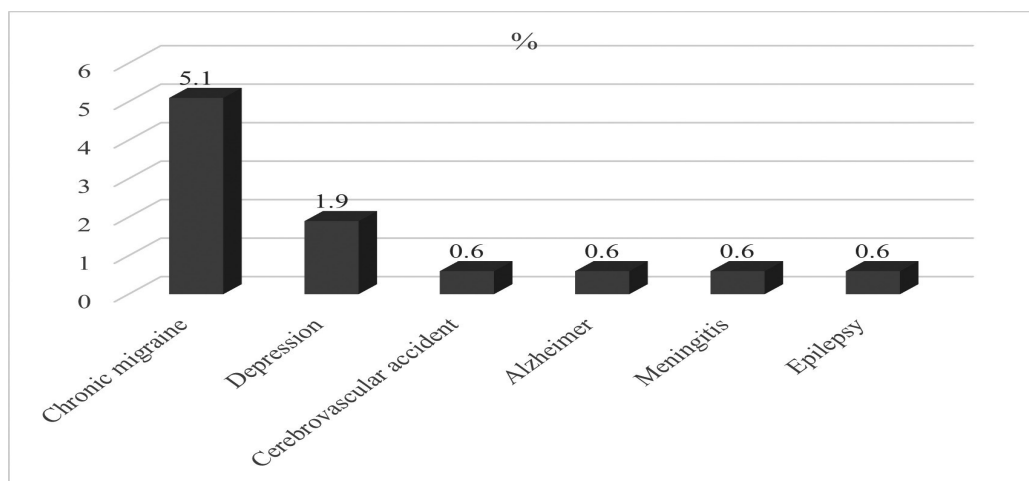**Figure 4.** Distribution of associated digestives diseases

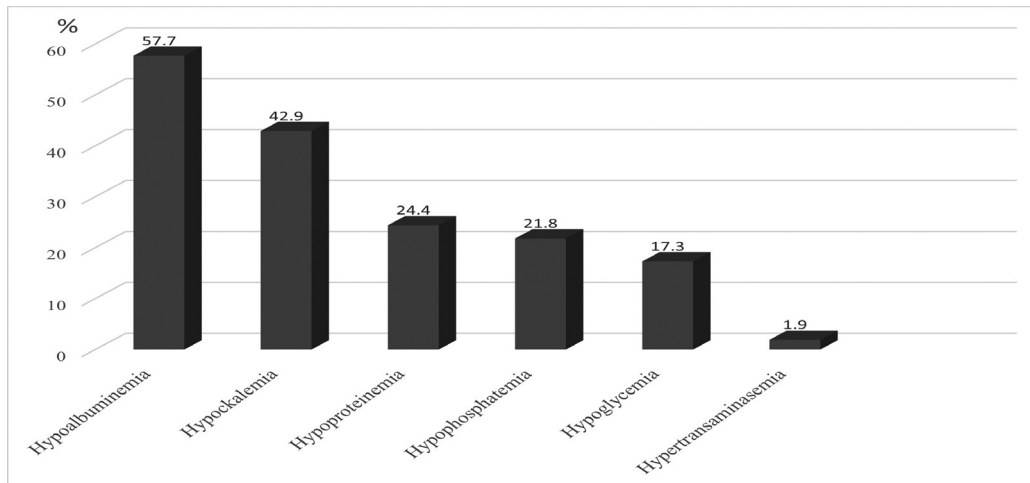 **Figure 5.** Distribution of associated nervous diseases

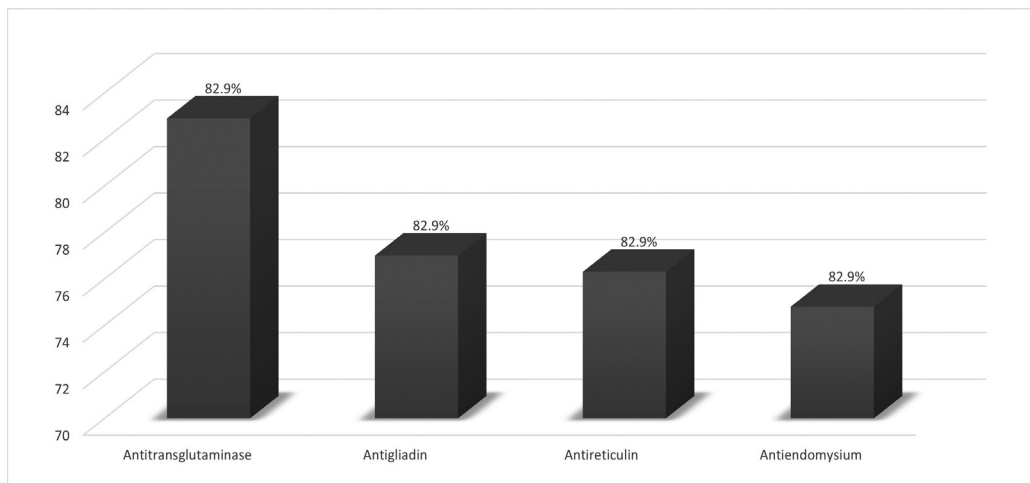**Figure 6.** Disruption of perturbation of biochemical markers

Figure 7. Distribution of positivity of serum antibodies.

Table 1. Relationship between serum antibodies and grades of the disease

Grade	anti-tTG2 Total n=102		antigliadin antibodies Total n=117		anti endomysial antibodies Total n=98		antiretuculin antibodies Total n=54	
	Negative	Positive	Negative	Positive	Negative	Positive	Negative	Positive
Grade 1	0	1	0	1	0	1	0	1
Grade 3	6	21	7	26	10	17	5	9
Grade 4	6	9	7	10	6	9	4	3
Grade 5	5	54	17	54	9	46	3	29
Total	17	85	26	91	25	73	12	42

Discussion

To demonstrate the clinical spectrum of CD, the iceberg model is commonly used. The incidence of CD here relates to the total size of the iceberg, while the area above the waterline-the tip of the iceberg-represents the number of clinically diagnosed cases. The area below the waterline at a certain point in time indicates the total number of undiagnosed cases in a given population [9]. This means that without active screening, most cases of celiac disease would remain undetected [7]. With a prevalence of 0.5% to 1% in both adults and children in the population, screening studies have shown that CD is seriously underdiagnosed [10-14] partly because its variable clinical presentation and symptoms are also not understood by doctors

[15].

On the other hand, the clinical picture of the disease can vary over the life of the same patient. In any of the countries or geographical areas in which epidemiological studies have been carried out, there are no substantial differences between symptomatic patients and "screened" patients [7].

CD is a widespread but often unrecognized disease. There is a predominance of women, with a 2-3:1 female-to-male ratio [16]. We noted a female to male ratio of 1.4:1 in our research. For unknown reasons, among adults, two to three times as many women have the disease compared to men. In general, the prevalence of autoimmune disorders is higher in women than in men, and iron deficiency and osteoporosis are more frequently diagnosed in women, both of which necessitate screening for celiac disease. The prevalence of the disease in women, however, decreases considerably after 65 years of age [17].

Depending on the age group, clinical types of celiac disease vary greatly. Diarrhea, abdominal distention, and failure to thrive are commonly observed in infants and young children. However, it is also normal to experience irritability, anorexia, vomiting and even constipation. Older children and teenagers also have extra-digestive symptoms, such as anemia, neurological symptoms, or small stature [18]. Diarrhea, which may be accompanied by abdominal pain or discomfort, is a common symptom for adults. However, in less than 50% of cases in the last decade, diarrhea has been the main presenting symptom [19]. Such silent presentations in adults include iron-deficiency anemia, osteoporosis, and the identification of unintended endoscopy for other purposes, such as symptoms of gastroesophageal reflux [20]. Abdominal pain, constipation, neurological symptoms, weight loss, hypocalcemia, hypoproteinemia, dermatitis herpetiformis and elevated liver enzyme levels are less common [6].

The results of the present study are comparable to this data. We noted a variety of signs, gastrointestinal symptoms which were represented mainly by abdominal pain and chronic diarrhea, and extra-intestinal symptoms which were represented mostly by weight loss, pallid skin and mucosa, and asthenia. In addition

to digestive and extra-digestive symptoms, celiac disease in our sample may be associated with biological disturbances, especially hypocalcemia resulting from inadequate absorption.

Some CD cases are diagnosed in people with a family history of the disease and in those with type 1 diabetes, Turner syndrome or Down syndrome, both of which are associated with celiac disease, due to increased screening for celiac disease [21-24]. In our simple, associated pathologies were represented mainly by anemia (67.9%) and digestive diseases (38.46%), and 17.3% and 16.7% of the patients had mouth ulcers and type 1 diabetes, respectively. The association between type 1 diabetes and CD can be explained with the increased risk of autoimmune disorders in celiac disease compared with the general population [25, 26].

One of the reasons for incorrect diagnosis of the disorder is the heterogeneity of its clinical manifestations. Currently, the cause of this diversity of symptoms is not known, but there is some evidence that both environmental and genetic factors may be involved [27, 28]. Some studies have shown that the gene dose impact is substantially correlated with the heterogeneity of clinical diseases [27, 29]. However, others have not noted a relationship [30].

Conclusions

In conclusion, CD reveals a complicated clinical spectrum and is one of the most common chronic gastrointestinal disorders of today. The disease represents a growing public health problem and preventive strategies are warranted.

In adults in eastern Algeria, this disease can be determined by a multitude of digestive symptoms mainly by abdominal pain and extraintestinal disorders which presented mainly with weight loss, pallid skin and mucosa and asthenia, in addition to a series of associated conditions. A prospective large-scale and multicenter study should be carried out in the future to further validate our findings.

Conflict of interest

The authors note that they have no conflicts of interest associated with this paper.

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