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Epidemiological, Clinical, Histological, Serological and Therapeutic Study of Children Celiac Disease in Western Algeria Region

Dounia Zad EL MEHADJI[1]*, Khalida ZEMRI[1], Hayet MEHIDA[1], Noria HARIR[1], Djamila YEKROU[2], Karim Bouziane NEDJADI[3], Charef LATROCH[3], Siheme OUALI[1], Zahira BENAISSA[1]

[1]. Laboratory of Molecular Microbiology, Proteomics and Health. Department of Biology, Djillali Liabes University of Sidibel Abbes, (Ex ITMA), Algeria
[2]. Departement of Medical Oncology, Anti-Cancer Centre of Sidi Bel Abbes. Algeria
[3]. Departement of Pediatrics « C »(A. Cabral), CHU of Oran, Algeria

ABSTRACT

Objectives: To determine the epidemiological, clinical, histological, serological and therapeutic profile of celiac disease in children in Western Algeria region.
Methods: 250 patients over a period of three years (2016 - 2019) from the pediatric department of the University Hospital of Oran (West Algeria) were included in our retrospective study.
Results: We noticed a female predominance with a sex ratio F/M = 1.57. Symptoms were defined by typical (73.2%) and atypical (26.8%) forms, digestive disorders (47.2%), extra digestive disorders (14.4%). Anemia was noted at 73.6%, and the association with autoimmune diseases at 14.8%. Seropositivity was present in 77.6% of cases and histology revealed partial grade villous atrophy at 54%. We noticed a significant link between the histological grade and the serology ($p = 0.001$), between age and histological grade ($p<10^{-3}$), between bone age and body mass index ($p = 0.017$), between the age of onset of the disease and the age of food diversification ($p = 0.030$), and with the age of breastfeeding ($p = 0.026$). In addition, we found an excellent correlation between anti-transglutaminase and anti-endomysium autoantibodies during diagnosis and under diet ($p<10^{-3}$), and between serology during diagnosis and serology under diet ($p = 0.002$)
Conclusion: Celiac disease (CD) of children in western Algeria is characterized by a variety of clinical symptoms. The gluten-free diet remains the only therapy for these affected children.
Keywords: celiac disease, children, epidemiology, serology, histology, associated diseases, treatment.

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***Address for Correspondence:**

Dounia Zad EL MEHADJI, PhD Candidate in Biochemistry-Immunology, Laboratory of Molecular Microbiology, Proteomics and Health. Department of Biology, Djillali Liabes University of Sidibel Abbes, (Ex ITMA), Algeria

INTRODUCTION

Celiac disease is an autoimmune-mediated enteropathy, which occurs in genetically susceptible individuals [1]. It is a chronic, systemic and inflammatory pathology characterized by villous atrophy of the small intestine induced by a food antigen, prolamins (gluten) [2, 3]. The frequency of the disease is worldwide even if the disease goes undiagnosed [4], the incidence of the disease has increased in recent decades. Celiac disease is a major public health problem affecting 1% - 3% of children [5, 6]. According to screening studies in children, the prevalence varies between 3 and 14/1000 [7, 8] while in Sahrawi children in Algeria the prevalence is exceptional, it is 56/1000 [9]. This disease manifests itself at any age and the clinical presentation is defined by a variety of symptoms [10]. The symptomatologies of the disease of classic form are the most typical and are defined by the gastrointestinal manifestations (GT), but also, can have extra intestinal manifestations [11-13]. Through this study we aim to understand the parameters identifying this disease nevertheless the epidemiological, serological, clinical and histological profile in children of the region of Western Algeria.

PATIENTS AND METHODS

The population:

We have established a retrospective epidemiological study, in the pediatric department, Saint-Michel, of Oran region (western Algeria), bringing together 250 patients with celiac disease over a period of three years (2016-2019). Only CD children having performed serological and histological analyzes and aged less than 16 years were included in our survey. The following variables were considered: age; sex; disease duration; serological and histological assessment; comorbidities; age of disease onset; the age of the gluten-free diet; age of dietary diversification and the age of introduction of gluten; and treatments.

The statistical analysis:

Concerning the statistical analytical study, data were summarized using rates and cross-tabulations. For the Associations between different parameters the Pearson's Khi2 test (χ^2) was used to evaluate the statistical significance (P<0.05). All data were processed and analyzed via SPSS 22.0 **(Statistical Package for the Social Sciences, IBM Corporation; Chicago, IL. August 2013).**

RESULTS:

250 cases were enrolled in our study between 2016-2019 (61.2% females and 38.8% males). A clear female predominance was noted with the female to male ratio of 1.57, the median age was of 5.10±3.82 running from 6 month to 13 years old.

In our population, the average age of onset of the disease was at 3.44 ± 3.34 years, while that of introduction of gluten was at 6.37 ± 2.19 months. However, the average age at the start of dietary diversification in our children was at 5.36 ± 1.58 months.

Birth weight was within range for all patients and the median body mass index was at 15.32 ± 2.57kg / m2. 25% of celiac children were from consanguineous marriage and 24.4% had a family history of the disease (Table 1).

Celiac disease was typical in 73.2% of cases and atypical in 26.8%. Symptoms were defined as digestive disorders (47.2%): chronic diarrhea 64.8%, abdominal pain 52.4%, vomiting 37.6% and abdominal bloating in 34.4% of cases. Extra digestive manifestations were noted in 14.4% of patients: such as weight loss at 38.4%, anemia at 30% and failure to thrive at 35.6%. Bone age was consistent with chronological age in 60% of the children.

Pathological examination of the duodeno-jejunal biopsy showed the presence of partial grade villous atrophy at 54%, subtotal at 23.6% and total at 12%. According to Marsh's classification, stage 3 was dominant in 29.2% of patients, with a rate of intraepithelial lymphocytes greater than or equal to 30% in 46%. 77.6% of cases presented a positive serology. In fact, the seropositivity of the anti-transglutaminase isotype IgA, IgG auto-antibodies assay was noted in 68% and 76.8% respectively. Likewise, anti-gliadins of isotype IgA were positive at 88.4% and anti-endomysium in 87.6% of cases (table 2).

73.6% of the children developed anemia with an average hemoglobin (10.78 ± 1.77g / dl), 8% an allergy to cow's milk proteins (CMPA), 5.6% thyroid disorders and 2.4% asthma. However, we noted an association with autoimmune diseases at 14.8% (thyroiditis at 6.8%, Type I Diabetes at 3.2%,IgA deficiency at 2.8%,linear IgA dermatosis 1.2% and psoriasis at 0.8% of cases). The gluten-free diet was prescribed for all patients as the only treatment for this disease but sometimes combined with symptomatic treatments to treat digestive disorders and anemia. Almost 65.2% of cases followed the diet well and serological analysis after two years on the diet showed negativity in 76% of cases with an average body mass index of 17.20 ± 3.08kg / m2.

Statistical analysis showed the existence of a significantly increased correlation link between the origin and the socio-economic level of patients (p = 0.003), between bone age and body mass index (p = 0.017), between the age of onset of the disease and the age of food diversification (p = 0.030), and with the age of breastfeeding (p = 0.026). We also noted a correlation between age and histological grade (p<10-3). Likewise, a very significant correlation between age and age of disease onset (p<10-3), age and age of gluten-free diet (p<10-3) and also the age of disease onset was correlated with the age of onset of the gluten-free diet (p<10-3). In addition, we found an excellent correlation between anti-transglutaminase and anti-endomysium autoantibodies during diagnosis and under diet (p<10-3), and between serology during diagnosis and serology under diet (p = 0.002) (table 3).

Chi-square test also showed a significant association between histological grade and serology (p = 0.028) (figure1).

Table 1 : Characteristics of population

Number (%)	
Gender, n (%)	
Female	153 (61.2%).
Male	97 (38.8%).
Personal history, n (%)	
Medical staff, n (%)	
Anemia	20 (8%).
Notion of prematurity	14 (5.6%).
Type I diabetes	8 (3.2%).
Allergy	6 (2.4%).
Surgical personnel, n (%)	
Appendectomy	2 (0.8%).
Cholecystectomy	1 (0.4%).
Ectopitesticular	1 (0.4%).
Family history of CD, n (%)	61 (24.4%).
Consanguinity of parents, n (%)	63 (25.2%).
Socio-economic level n, (%)	
Good	26 (10.4%).
Bottom	70 (28%).
Medium	154 (61.6%).
CD: celiac disease	

Table 2 : Clinical, histological and serological characteristics of population

Clinical symptoms	Number (%)
Circumstances of Discovery	
Typical	183 (73.2%)
Atypical	67 (26.8%)
Symptomatology	
Digestive disorders	118 (47.2%)
Chronic diarrhea	162 (64.8%)
Abdominal pain	131 (52.4%)
Vomitings	94 (37.6%)
Abdominal bloating	86 (34.4%)
Constipation	35 (14%)
Abdominal Distention	15 (6%)
Nausea	13 (5.2%)
Epigastralgia	6 (2.4%)
Extradigestives	36 (14.4%)
Weight loss	96 (38.4%)
Anemia	75 (30%)
Staturo-ponderal delay	89 (35.6%)
Pallor	62 (24.8%)
Asthenia	38 (15.2%)
Anorexia	19 (7.6%)
Mouth ulcer	11 (4.4%)
Weakness and muscle cramps	10 (4%)
Skin rash	10 (4%)
Edema	2 (0.8%)
Digestive disorders and Extra digestives	96 (38.4%)
Histology	
Villous atrophy	
Presence	250 (100%)
Grade of atrophy	
Partial	135 (54%)
Partial to subtotal	26 (10.4%)
Subtotal	59 (23.6%)
Total	30 (12%)
Marsh Classification	
2 to 3	43 (17.2%)
3	73 (29.2%)
3a	17 (6.8%)
3 to 4	26 (10.4%)
3b	13 (5.2%)
3c	10 (4%)
4	46 (18.4%)
4 to 5	9 (3.6%)
5	13 (5.2%)
LIE ≥30%	115 (46%)
Serology	
Doubtful	11 (4.4%)
Positive	194 (77.6%)
Negative	45 (18%)

Autoantibody assay n,(%)	Doubtful	Negative	Positive
tTG-IgA	8(3.2%)	72 (28.8%)	170 (68%)
tTG-IgG	6 (2.4%)	52 (20.8%)	192 (76.8%)
AGA-IgA	3 (1.2%)	26 (10.4%)	221 (88.4%)
EMA-IgA	3 (1.2%)	28 (11.2%)	219 (87.6%)

Table 3: the correlation between the age of onset of the disease and different parameters

Variable	Age of onset of the disease		
	n	r (corrélation coefficient)	p
Age of dietary diversification	250	0.137*	0.030
Breast feeding age		0.141*	0.026
Age on Gluten-Free Diet		0.703**	$<10^{-3}$
	Age range		
Age of onset of the disease	250	0.670**	$<10^{-3}$
Histological grade		0.270**	$<10^{-3}$
Age on Gluten-Free Diet		0.765**	$<10^{-3}$
Origin			
Socio-economic level	250	0,187**	0,003
bone age			
Body mass index	250	-,152*	0,017
Anti-transglutaminase			
Anti-endomysial	250	0,746**	$<10^{-3}$
Serology under regimen			
Serology at diagnosis	250	0,198**	0,002

*. The correlation is significant at the 0.05 level (two-way). **. The correlation is significant at the 0.01 level (two-way).

Chi-square test shows a significant association between associated diseases and associated autoimmune diseases($p<10^{-3}$),The results are not significant between symptomatology and histology, histological grade and serology(p=0.028) Figure 1 illustrates the significance between serology and histology

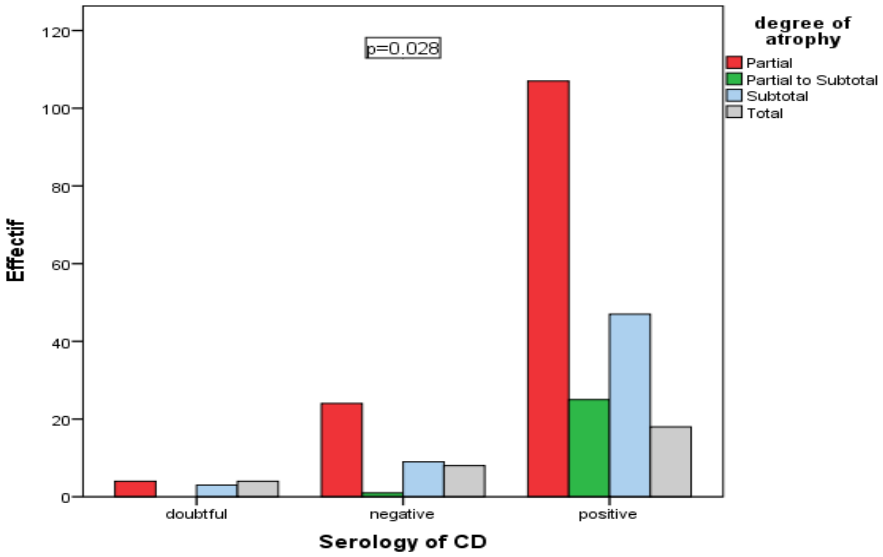

Figure 1: Distribution of patients according to significance between serology and histology

DISCUSSION

At the end of our study, celiac disease was characterized by a clear predominance of the female sex with a sex ratio of 1.57. This predominance was also underlined by other studies [14]. Celiac disease can be diagnosed at any age but presents as an atypical form in adolescents and adults [10]. In our study, the mean age of onset of the disease was 3.44 ± 3.34 years which agrees with the results of [15] in eastern Algeria. Nevertheless, the diagnosis of the disease is essentially based on a recombination of histological, serological, clinical criteria and the response to the gluten-free diet [12, 16]; this was well indicated and confirmed by our results. The literature suggests that the symptomatology of the disease appears in children when gluten is introduced and more precisely at the age of onset of dietary diversification as well as when breastfeeding is stopped [15, 17] which is consistent with our results. Thus, breastfeeding plays a protective role against this pathology.

The clinical presentation showed the predominance of the classic (typical) form, at 73.2%, while the atypical form was noted at 26.8%, characterized by gastrointestinal or extra-intestinal manifestations, respectively. This result is consistent with the data noted in the studies of A. S. McNeish *et al* [16] and J. F. Ludvigsson *et al* [18]. Chronic diarrhea (64.8%) and abdominal pain (52.4%) and vomiting (37.6%) were the most frequent disorders in our sample, which is in agreement with a study conducted in Sudan which noted chronic diarrhea as the main characteristic of the disease in children [19]. However and in a comparable way in the region of eastern Algeria, children presented abdominal pain as the main symptom [15]. The disease is defined by a diversity of symptoms, mainly digestive disorders, these data are also confirmed by our results [15, 20]. In addition, and in association with digestive disorders, we particularly observed the symptoms of weight loss at 38.8%, anemia at 36.8%, failure to thrive at 36% and mucocutaneous paleness at 25.6%.

Which confirms that celiac disease can manifest itself from intestinal or extra intestinal manifestations [11] in children and Adolescents.

Celiac disease promotes the development of many pathologies, the most common in our series was anemia at 73.6%. These data are similar to those of [21, 22]. Therefore, our results underline that anemia is a complication of celiac disease, which can be either related to nutritional status (weight loss) or to hematological disorders [23]. CD was associated with more than one autoimmune disease defining multiple autoimmune syndrome, its association with autoimmune diseases is highlighted primarily with type I diabetes and thyroiditis as reported in the literature [1, 24].

This study confirms that the histological examination is the main test and is done by a duodenojejunal biopsy. Partial grade villous atrophy and Marsh classification 3 was noted in most of our patients, confirming the results of the study by [25]. Likewise, serological tests are considered to be the most reliable for detection of the disease and even are recommended in screening [26]. Indeed, the positivity of the serology is essential for the diagnosis to be acquired. In our work, this positivity was found in 77.6% of patients. We noticed a significant link between the histological grade and the serology (p = 0.001), which is consistent with the findings of the study conducted in eastern Algeria [15]. Similarly, an excellent correlation between anti-transglutaminase and anti-endomysium autoantibodies has been revealed, which confirms their specificity and sensitivity, thus joining the results of P. Roujon *et al* [27].

The treatment of the disease is based on diet, in our study all the patients were advised to follow a gluten-free diet. According to the literature, the gluten-free diet remains the only effective treatment for the disease but remains difficult to maintain [26, 28]. Compliance with the gluten-free diet was assessed by self-report of patients with reported deviations from the diet and by the presence of clinical signs.

CONCLUSION:

According to our results, the clinical presentation of celiac disease in Algerian children (west Algeria) is also defined by typical and atypical forms with intestinal or extra intestinal symptoms respectively and the gluten exclusion diet remains the major element for the success of the dietary management. A prospective study should be carried out at the long term in different regions of our country to validate and compare the different characteristics of celiac disease in children, as well as to study the factors predisposing the Algerian population to this pathology.

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