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**Research Article** 

# Comparative Profile of Celiac Disease Between Children and Adults in Western Algeria Region

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#### Abstract

**Background:** This study was performed to describe the main differences and similarities of celiac disease according to age and highlight the clinical features, diagnosis, associations of the disease, complications, and response to a gluten-free diet in children and adults.

**Methods:** A retrospective study was conducted on a series of patients (n = 223) diagnosed with celiac disease during infancy (< 2 years) and childhood ( $\geq$  2 years) versus a series of adult patients ( $\geq$  17 years).

**Results:** A total of 223 patients were included in this study, 40, 109, and 74 of whom were infants, children, and adults, respectively. The age of diagnosis was delayed in adults, with a mean value of  $21.07 \pm 12.49$  years versus  $03.37 \pm 3.93$  and  $6.53 \pm 3.77$  years in infants and children, respectively (P< 0.001). The clinical manifestations in infants and children were defined as digestive disorders, mainly chronic diarrhea (P = 0.004), similar in adults. Nevertheless, the extra digestive manifestations were predominant in adults, and anemia was the most frequent manifestation (51.4%) versus 30% (n = 12) and 33.9% (n = 37) in infants and children, respectively (P = 0.026), while weight loss in adults affected 52.7% (P for the difference between the three age groups = 0.004). In adults, there was a higher frequency of associated autoimmune diseases, including hypothyroidism (8.1% versus 4.6% in children), Crohn's disease (5.4% versus 0.0% in children), and lupus (0.9% versus 0.0% in children) (P < 0.001). Serology was strongly positive in all three age groups but with no significant difference between them (P = 0.184). The difference between the three age groups concerning the immunoglobulin G (IgG) anti-transglutaminase (a-tTG) assay positivity was statistically significant (P < 0.001). The partial grade of villous atrophy was dominant in all three groups. Good adherence to the diet was more noticeable in children than adults (P = 0.001).

**Conclusions:** Celiac disease presents differences between adults and children. The atypical clinical presentation is dominant in adults. Children present a positive serology and good adherence to the diet.

Keywords: Comparative Profile, Adults, Children, Diet Adherence, Clinical Symptoms, Celiac Disease

#### 1. Background

Celiac disease or gluten-sensitive enteropathy is a chronic inflammatory systemic disease of autoimmune origin in genetically predisposed individuals (1). Celiac disease affects approximately 1 - 2% of the general population of all races and countries, with a homogeneous distribution worldwide, and diminishes with age (2, 3). Celiac disease leads to important morbidity but very low mortality (4).

Celiac disease can be diagnosed at any age (5). The

disease is seen in both children and adults, and most individuals consider the disease in children and adults to be basically the same (4, 6). Pediatric celiac disease is characterized by predominantly digestive characteristics with a typical malabsorption syndrome associated with digestive disorders (7). Nevertheless, adult celiac disease is presented in atypical forms characterized by extra digestive symptoms (5, 8).

The current diagnostic strategy for celiac disease is based on clinical suspicion and confirmed by serological

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and histological tests. However, the screening and diagnosis of celiac disease are relatively well-established (9, 10). The treatment of celiac disease is essentially based on a gluten-free diet that remains the only effective treatment (11).

# 2. Objectives

This study aimed to describe the main differences and similarities of celiac disease according to age and highlight the clinical features, diagnosis, associations of the disease, complications, and response to a gluten-free diet in infants, children, and adults.

## 3. Methods

A cross-sectional observational study was conducted on 223 patients diagnosed with celiac disease in the Pediatrics Department of the Oran University Hospital Center and the Gastroenterology Department of Tlemcen University Hospital Center (Western Algeria). The patients' recruitment was carried out at the level of (1) the Pediatrics Department of the Oran University Hospital Center; (2) the Gastroenterology Department of Tlemcen University Hospital Center; and (3) the National Association of Celiac Protection in the Sidi Bel Abbes. Three groups were selected according to age, including infants < 2 years, children or adolescents  $\geq 2$  years, and adults  $\geq 17$  years. The current epidemiological survey was conducted over 2 years (2019-2021). The data were collected from the records of celiac patients and, according to the inclusion criterion, a histological and/or serological diagnosis of the disease with full respect for the confidentiality of the data and patients. All celiac cases lost to follow-up were excluded. The aforementioned criteria were applied to both genders and all age categories.

# 3.1. Statistical Data

The description, processing, and analysis of statistical data in the studied sample were carried out via SPSS software (version 22.0; Statistical Package for the Social Sciences, IBM Corporation; Chicago, IL. August 2013). Moreover, the data were presented in rates The results were expressed and cross-tabulations. as frequencies, means, and standard deviations. Α Pearson's chi-square test ( $\chi^2$ ) was used to evaluate clinical symptoms and diseases associated with celiac disease according to the age group, and ANOVA test to evaluate an anthropometric parameter according to the age group. The statistical level of significance was P < 0.05. The reference values for the comparison between age groups were made using a 95% confidence interval.

# 4. Results

Among the 223 celiac patients enrolled in this study, 40 (17.9%), 109 (48.9%), and 74 (33.2%) subjects were infants < 2, children  $\geq$  2, and adults  $\geq$  17 years, respectively. There was a predominance of female gender with a gender ratio of 1.62. The average age was 15.17  $\pm$  15.76 years in all patients, with 1.68  $\pm$  0.38, 7.04  $\pm$  3.68, and 34.44  $\pm$  12.66 years in infants, children, and adults, respectively. A significant difference was noted in this regard (P < 0.001). The mean values of age at diagnosis and age of gluten-free diet were 10.79  $\pm$  10.72 and 9.23  $\pm$  9.93 years in all patients, respectively. A significant difference was observed in this regard (P < 0.001).

The mean body mass index (BMI) in the studied sample was  $15.79 \pm 2.47 \text{ kg/m}^2$ . The mean BMI values of children, adults, and infants were  $15.13 \pm 1.99$ ,  $16.74 \pm 3.03$ , and  $15.86 \pm 1.90 \text{ kg/m}^2$ , respectively, with a significance of P < 0.001 in all age groups. The average hemoglobin level at diagnosis in all patients was  $10.63 \pm 1.89 \text{ g/dL}$ , with  $10.66 \pm 1.89$ ,  $10.66 \pm 2.00$ , and  $10.52 \pm 1.73 \text{ g/dL}$  in children, adults, and infants, respectively, with no significant difference between the three age groups (P = 0.92) (Table 1).

The symptomatological diversification assessment showed that the clinical features of the disease were defined as digestive disorders (n = 109, 48.9%) in all patients, with 56 (25.1%), 29 (13.0%), and 24 (10.8%) subjects in children, adults, and infants, respectively. The most common digestive disorder noted in the children group ( $\geq$  2 years) were chronic diarrhea, abdominal bloating, abdominal pain, and vomiting in 59 (54.1%) (P = 0.004), 35 (32.1%) (P < 0.001), 64 (63.3%) (P = 0.026), and 39 (35.6%) (P = 0.183) patients, respectively. However, vomiting was frequent in infants (< 2 years) with 52.5%. Nevertheless, abdominal distension and epigastralgia were the most frequent digestive disorders noted in adults, with a frequency of 19 (25.7%) (P = 0.001) and 3 (4.1%) (P = 0.442) patients, respectively.

Weight loss (52.7%), anemia (51.4%), and asthenia (37.8%) were the main extra digestive disorders in the adult group, with statistically significant differences of P = 0.026, P = 0.008, and P = 0.004, respectively. However, stunting was the most extra digestive disorder noted in the children group, with a frequency of 32.1% and a significant difference of P = 0.016. Nonetheless, in the infant group, anemia was the most frequent extra digestive disorder in 39% of the patients (Table 2).

The comorbidity of celiac disease in the patients was noted in this study. An anemia rate of 16.5% was observed in the children group. Nevertheless, a hypothyroidism rate of 8.1% was noticed in the adult group. Other autoimmune diseases were also noted in the adult group as Crohn's

Characteristics	All Patients (n=223)	CI 95%	Infants (< 2 Years) (n	CI 95%	Children (≥ 2	CI 95%	Adults ( $\geq$ 17 Years) (n	CI 95%	P-Value	P-Value
			=40)		Years)(n = 109)		=74)			
Age (y)	15.17±15.76	13.09 - 17.25	1.68± 0.38	1.56 - 1.81	7.04 ± 3.68	6.34 - 7.74	34.44 ± 12.66	31.51 - 37.38	< 0.001 <sup>b</sup>	< 0.001 <sup>C</sup> (infants vs. children); < 0.001 <sup>C</sup> (infants vs. adults); < 0.001 <sup>C</sup> (adults vs. children)
Age at first diagnosis (y)	$10.79\pm10.72$	9.37 - 12.20	03.37±3.93	2.11 - 4.63	6.53±3.77	5.81 - 7.24	21.07±12.49	18.18 - 23.97	< 0.001 <sup>b</sup>	0.68 (infants vs. children);< 0.001 <sup>C</sup> (infants vs. adults);< 0.001 <sup>C</sup> (adults vs. children)
Age of gluten - free diet (y)	9.23±9.93	7.92 - 10.54	$1.80\pm0.68$	1.58 - 2.02	5.94±3.37	5.30 - 6.58	18.09±12.52	15.19 - 20.99	< 0.001 <sup>b</sup>	0.08 (infants vs. children); < 0.001 <sup>C</sup> (infant vs. adults); < 0.001 <sup>C</sup> (adults vs. children)
BMI (kg/m <sup>2</sup> ) during the diagnosis	15.79 ± 2.47	15.47 - 16.12	$15.86\pm1.90$	15.25 - 16.47	15.13 ± 1.99	14.75 - 15.51	$16.74\pm3.03$	16.03 - 17.44	< 0.001 <sup>b</sup>	0.197 (infants vs. children); 0.114 (infants vs. adults); < 0.001 <sup>C</sup> (adults vs. children)
Hb (g/dL) during the diagnosis	10.63± 1.89	10.38 - 10.88	10.52±1.73	9.97 - 11.08	10.66±1.89	10.30 - 11.01	10.66± 2.00	10.19 - 11.12	0.92	0.916 (infants vs. children); 0.943 (infants vs. adults); 0.998 (adults vs. children)

Abbreviations: BMI, body mass index; Hb, hemoglobin; CI, confidence interval; SD, standard deviation. <sup>a</sup> Values are expressed as mean ± SD unless otherwise indicated. <sup>b</sup> Significant level of analysis of variance (P < 0.05). <sup>c</sup> Significant level of Tukey's post-hoc test.

Characteristics	All Patients (n = 223)	Infants (< 2 Years) (n = 40)	Children (≥ 2 Years) (n = 109)	Adults ( $\geq$ 17 Years) (n = 74)	P-Value
Digestive disorders					
Chronic diarrhea	142 (63.7)	33 (82.5)	59 (54.1)	50 (67.6)	0.004 <sup>b</sup>
Abdominal bloating	55 (24.7)	17 (42.5)	35 (32.1)	3 (4.1)	< 0.001
Abdominal pain	142 (63.7)	19 (47.5)	64 (63.3)	54 (73.0)	0.026 <sup>b</sup>
Constipation	28 (12.6)	6 (15.0)	19 (17.4)	3 (4.1)	0.024 <sup>b</sup>
Vomiting	90 (40.4)	21 (52.5)	39 (35.8)	30 (40.5)	0.183
Abdominal distension	30 (13.5)	3 (7.5)	8 (7.3)	19 (25.7)	0.001 <sup>b</sup>
Epigastralgia	06 (2.7)	0 (0.0)	3 (2.8)	3 (4.1)	0.442
Extra digestive disorders					
Anemia	87 (39)	12 (30)	37 (33.9)	38 (51.4)	0.026 <sup>b</sup>
Anorexia	23 (10.3)	6 (15.0)	11 (10.1)	6 (8.1)	0.511
Asthenia	56 (25.1)	7 (17.5)	21 (19.3)	28 (37.8)	0.008 <sup>b</sup>
Staturo-ponderal delay	56 (25.1)	11 (27.5)	35 (32.1)	10 (13.5)	0.016 <sup>b</sup>
Weight loss	90 (40.4)	19 (47.5)	32 (29.4)	39 (52.7)	0.004 <sup>b</sup>
Pallor	63 (28.3)	12 (30.0)	25 (22.9)	26 (35.1)	0.191
Weakness and muscle cramps	23 (10.3)	1(2.5)	6 (5.5)	16 (21.6)	< 0.001
Depressed state	5(2.2)	0 (0.0)	1(0.9)	4 (5.4)	0.075
Skin rash	13 (5.8)	3 (7.5)	2 (1.8)	8 (10.8)	0.035 <sup>b</sup>
Splenomegaly	2(0.9)	0 (0.0)	0 (0.0)	2 (2.7)	0.131
Oral aphthosis	7 (3.1)	2(5.0)	2 (1.8)	3 (4.1)	0.530

<sup>a</sup> Values are expressed as No. (%). <sup>b</sup> Significant.

disease (5.4%) and lupus (0.9%), with a significant difference (P = 0.001). However, allergy was present in the infant group with 22.5% (Table 3).

The results of serological tests of all patients with positive disease serology were 90.0% and 80.7% in infants and children, respectively, versus 89.2% in the adult group. No significant difference was recorded with serology (P = 0.184). This study also determined differences in the frequency of immunoglobulin G (IgG) at anti-transglutaminase (a-tTG) refers to assay positivity (P < 0.001) for all age groups. However, the immunoglobulin A-type (IgA) assay positivity was dominant in all the age groups.

The histological examination (at the time of diagnosis) according to the degree of severity of the lesion of the intestinal mucous membrane showed that 45.3% were grade partial villous atrophy. It was predominant in adults at 48.6% vs. 47.5% and 42.2% in infants and children, respectively. The total grade was dominant in adults (18.9%). There was no significance between the three age groups (P = 0.097) (Table 4).

The gluten-free diet with good adherence was noted in 63.2% of all patients, with 62.5% and 74.3% in infants and children, respectively, versus 47.3% in adults. There was a significant difference in this regard (P = 0.001).

### 5. Discussion

The current study analyzed the differences between pediatric and adult celiac disease, and the obtained results showed that pediatric and adult celiac disease is characterized by a female predominance in all age groups with a gender ratio of 1.62. This predominance was also suggested by other studies (12, 13). In the present series, the mean age of celiac patients was  $15.17 \pm 15.76$  years. The mean age at disease diagnosis was 10.79  $\pm$  10.72 and 21.07  $\pm$ 12.49 years in children and adults, respectively. This issue is confirmed by other studies (14), as the disease can be diagnosed at any age. Therefore, the starting age for the gluten-free diet was 9.23 ± 9.93 years in all patients and 1.80  $\pm$  0.68 years in infants. This suggests that the development of the disease is related to the cessation of breastfeeding and the early introduction of cereals containing gluten, confirmed by Poddar's study results (6).

The mean BMI in the current sample was  $15.79 \pm 2.47$  kg/m<sup>2</sup>; all the patients were malnourished (BMI < 16.5 kg/m<sup>2</sup>). This finding is similar to the findings of other studies conducted on Indian children indicating that growth retardation was a frequent manifestation of the disease (6). In a comparable way to adults, the present study's results demonstrated an increase in the rate of BMI (> 16.5 kg/m<sup>2</sup>) comparable to a study by Dickey and

Kearney (15), who showed that few celiac patients were underweight at diagnosis.

The clinical symptomatology of the disease was characterized by classic forms that are defined as digestive disorders, which were predominant in children (69%), mainly chronic diarrhea (54.1%), abdominal pain (63.3%), and abdominal bloating (32.1%), with a significant difference (P = 0.004; P = 0.026, and P < 0.001, respectively), which is consistent with a study by Rodrigo-Saez et al. (16) who noted that chronic diarrhea was the main feature of the disease in children. On the other hand, adults also expressed chronic diarrhea as the main symptom of the disease. The current study's results are confirmed by Sood et al.'s study (17), in which chronic diarrhea was present in adults, in contradiction with other studies' results (18). Therefore, the present study's results underline that extra digestive manifestations are quite common in adults with celiac disease, such as weight loss (52.7%), anemia (51.4%), and asthenia (37.8%), with a significant difference (P = 0.004, P = 0.026, and P = 0.026, respectively). The current study's results are suggested by several compliance studies (6). Although weight loss was the principal extra digestive manifestation (P = 0.004) in the infant group, the stature weight delay was dominant in children (P = 0.016). The aforementioned data are similar to those of Vivas et al.'s study (18).

In the present study, there were many diseases associated with celiac disease in children and adults; however, in the adult group, Crohn's disease and hypothyroidism seem to be more frequent, as noted in the results of studies by Doya et al. (19) and Baharvand et al. (20). Rodrigo-Saez et al. (16) suggested that most associated diseases in adults are of autoimmune origin. Unlike in the infant group, where allergy was followed by anemia as the main associated disease, Vivas et al. (18) suggest that anemia is one of the associated diseases in infants and children. Anemia, hypothyroidism, and type 1 diabetes were the main associated comorbidities confirmed by the results of El Mehadji et al.'s study (21). In addition, the literature has shown that celiac disease is associated with autoimmune diseases, mainly type 1 diabetes and hypothyroidism (22, 23).

The serological tests were necessary for the diagnosis of the disease, although the current study's results showed that serology was positive in 85.2% of celiac patients. The present study's results are similar to the results of other studies (21, 24), recalling that even in infants (90.0%), children (80.7%), and (89.2%) adults, the tests mainly (IgA and IgG a-tTG, IgA endomysial antibodies, and IgA antigliadin antibodies) were significantly higher for children than adults, which underlines an excellent predictive value to confirm the diagnosis (25, 26). A

Characteristics	All Patients (n = 223)	Infants (< 2 Years) (n = 40)	Children (≥ 2 Years) (n = 109)	Adults ( $\geq 17$ Years) (n = 74)	P-Value
Comorbidity					0.001 <sup>t</sup>
Allergy	15 (6.7)	9 (22.5)	6 (5.5)	0 (00.0)	
Anemia	28 (12.6)	8 (20.0)	18 (16.5)	2 (2.7)	
Asthma	4 (1.8)	1(2.5)	3 (2.8)	0(0.0)	
Type 1 diabetes	5 (2.2)	1(2.5)	4 (3.7)	0 (00.0)	
Lupus	2(0.9)	0 (00.0)	0 (00.0)	2 (0.9)	
Crohn's disease idism	4 (1.8)	0 (00.0)	0(00.0)	4 (5.4)	
Osteoporosis	2(0.9)	0 (0.0)	1(0.9)	1(1.4)	
Hypothyro	13 (5.8)	2(5.0)	5(4.6)	6 (8.1)	

 $^{\rm a}$  Values are expressed as No. (%).  $^{\rm b}$  Significant at P < 0.05.

Table 4. M	lain Diagnostic	Criteria	a
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Characteristics	All Patients (n = 223)	Children (< 2 Years) (n = 40)	Children (≥ 2 Years) (n = 109)	Adults ( $\geq$ 17 Years) (n = 74)	P-Value
Serological tests					
Positive	190 (85.2)	36 (90.0)	88 (80.7)	66 (89.2)	0.184
Negative	33 (14.8)	04 (10.0)	21 (19.3)	8 (10.8)	0.184
IgA a-tTG assay positivity (U/mL)	161 (72.2)	29 (72.5)	77 (70.6)	55 (74.3)	0.091
IgG a-tTG assay positivity (U/mL)	43 (19.3)	15 (37.5)	28 (25.7)	00(0.0)	< 0.001
IgA AGA assay positivity (U/mL)	86 (38.6)	21 (52.5)	40 (36.7)	25 (33.8)	0.145
IgA EmA assay positivity (U/mL)	20 (9.0)	05 (12.5)	08 (7.3)	07 (9.5)	0.609
Histological tests					0.097
Partial to subtotal	15 (6.7)	05 (12.5)	10 (9.2)	00(0.0)	
Partial	101(45.3)	19 (47.5)	46 (42.2)	36 (48.6)	
Subtotal	69 (30.9)	11 (27.5)	36 (33.0)	22 (29.7)	
Subtotal to total	02(0.9)	00(0.0)	00(0.0)	02 (2.7)	
Total	36 (16.1)	05 (12.5)	17 (15.6)	14 (18.9)	
Gluten-free diet adherence					0.001 <sup>b</sup>
Good adhesion	141 (63.2)	25 (62.5)	81 (74.3)	35 (47.3)	
Poor adhesion	82 (36.8)	15 (37.5)	28 (25.7)	39 (52.7)	

Abbreviations: IgA, immunoglobulin A-type; a-tTG, anti-transglutaminase antibodies; IgG, immunoglobulin G-type; AGA, antigliadin antibodies; EmA, endomysial antibodies.

<sup>a</sup> Values are expressed as No. (%).

<sup>b</sup> Significant at P < 0.05.

study by Roujon et al. (24) showed that anti-endomysium and tissue transglutaminase IgA antibodies represent the most specific and sensitive markers, with the exception of IgA-deficient patients. Further search for IgG is recommended. The present study's results are concordant with other studies' results (27) concerning the use of anti-transglutaminase assays. Nevertheless, the present study showed a significant difference in anti-transglutaminases of IgG (P < 0.001).

The histological test defined by a duodenal biopsy remains an examination of reference to confirm the diagnosis of celiac disease. That is why all the studied patients underwent a biopsy with the presence of villous atrophy of partial grade (Marsh = 3), which was dominant in all the patients. Moreover, the total grade (Marsh  $\geq$  3) was present in adults more frequently than in children. The aforementioned results were also reported by other studies (21, 27).

The response to the gluten-free diet is also necessary to confirm the diagnosis of celiac disease (26). Therefore, good adherence to the gluten-free diet was higher in children than in adults, with a significant difference (P = 0.001), which is consistent with another study's results (28). Poor adherence to the gluten-free diet and/or lack of clinical and histological response favors the development of refractory sprue, as confirmed by Leffler et al. (28) and Abdulkarim et al. (29).

# 5.1. Conclusions

Celiac disease in the western Algeria region presents many differences between children and adults. In adults, the presentation of the disease is marked during childhood and is characterized by the presence of atypical and typical forms. Additionally, comorbidity was in the form of autoimmune diseases in adults. Adherence to the gluten-free diet has been well established in children than adults.

### Footnotes

Authors' Contribution: Conception and design: Douniazad El Mehadji, Harir Noria, and Latroche Charef; administrative support: None; provision of study materials or patients: Douniazad El Mehadji, Harir Noria, Djamila Yekrou, Walid Hassene Hamri, and Siheme Ouali; collection and assembly of the data: Douniazad El Mehadji and Harir Noria; data analysis and interpretation: Douniazad El Mehadji, Harir Noria, Djamila Yekrou, Walid Hassene Hamri, and Siheme Ouali; manuscript writing: All authors; final approval of the manuscript: All authors.

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