Research Article
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Detection of celiac disease in a medicine student population

Summary

Introduction: Celiac disease affects 1-2% of the world population. The proportion of known versus undiagnosed cases is 1/3-10.

Goal: Characterize epidemiologically and clinically for celiac disease an university population of Medicine students.

Material and method: Data from the clinical history were collected in 638 students between 19 and 38 years. All of them were asked for general and specific laboratory analysis. Those with a high suspicion level of being celiac were asked for endoscopy and duodenum biopsy.

Results: Six with ninety-nine percent (6.99%) of the students with laboratory results were celiac confirmed by duodenal biopsy.

Sixty-eight eighty-four percent (68.84%) of the students were women, while among celiacs it was 92.31%.

Sixty-nine twenty-three percent (69.23%) of diagnosed as celiacs were within 50 and 80% of possibilities of being celiac.

The body mass index of celiacs was low weight, or at the lower limit of normal weight.

Thirty eight forty six percent (38.46%) of the celiacs with a positive biopsy had negative laboratory. Thirty seventy seven percent (30.77%) had low total IgA levels.

Fifty percent (50%) of the celiac and 7.37% in the general group had celiac relatives.

Conclusion: In 186 students with analysis, 6.99% celiac patients were found; therefore the biopsy is mandatory in adult population.

Four of ten students with positive biopsy had negative antibodies.

Celiac disease is a highly prevalent disease, with a heterogeneous clinical presentation which is usually under - estimated and under - diagnosed.

Early diagnosis is a priority in order to prevent complications and associated diseases.

Keywords: celiac disease, gluten, prevalence

Key concepts:

What is known: That Celiac Disease is under - estimated and under - diagnosed. The diversity of both digestive and extra-digestive symptoms makes diagnosis difficult and delayed.

What is new: This paper shows that if the disease is properly investigated it can reach a much higher prevalence. Those patients who go undiagnosed are at risk of serious irreversible complications and autoimmune diseases.

Disclosure paragraph

Celiac disease mainly affects the intestine and the whole organism in general. It is triggered by gluten found in grains such as wheat, oats, barley, and rye. It may have no symptoms, or multiple symptoms in each of the patient's devices and systems and is called the great simulator. The diagnosis is made through the clinical history, blood specific antibodies in the blood and upper digestive endoscopy with duodenal biopsy. His only treatment is a lifelong, strict gluten-free diet. In this group of university students, 6.99% of celiacs were diagnosed (the global prevalence is between 1 and 2% in most countries and different authors say that for every diagnosed celiac there are between 3 and 10 undiagnosed). Undiagnosed celiac patients are at risk of serious complications and other autoimmune diseases. For this, early diagnosis is very important.

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Introduction

Celiac disease (CD) is a complex multisystem disease, an autoimmune, chronic, hereditary enteropathy, triggered by an environmental (food) factor, such as gluten proteins present in cereals such as wheat, oats,[1] barley and rye.

The contact of gluten with the intestinal mucosa produces a characteristic damage that goes from the increase of the intraepithelial lymphocytic infiltrate (IEL)[2] to the total villous atrophy that produces a defect in the absorption of all the nutrients leading to deficiency states, in many cases responsible for a wide spectrum of clinical manifestations (gastroenterological and extraintestinal) and serious complications.[3] His only treatment is a strict, lifelong gluten-free diet (GFD).

It has a homogeneous worldwide distribution. There are no racial or age differences and the female/male ratio is 2-3/1.[4]

In recent years, the incidence of this disease has increased[5] and it is believed that the causes are the awareness of physicians that they should be alert to its varied symptoms (nonspecific and isolated symptoms and risk groups) and breadth of clinical presentations, the incessant search for atypical patients (such as adults, obese or with extraintestinal manifestations).[6] The appearance of the best tools for its detection, such as serology for anti EmA (endomysial), anti TtG (transglutaminase) and anti DGP (deaminated gliadin peptide) and genetic HLA (human leukocyte antigen) DQ2 and DQ8 antibodies and a real increase in cases of unknown cause.[7,8]

From the 2nd century BC there are written references that Cappadocia's Aretaeus (Roman doctor) called these paunchy children "koeliakos" (the one who suffers from the intestine) who consulted for abdominal pain.

The objective of this trial was:

- To characterize epidemiologically and clinically for CD a university population of Medicine students.

Material and method

Observational prospective study. 638 students of the Medicine career of Córdoba's National University (UNC) were included. Carried out in the Chairs of Medicine II and III Academic Unit of Internal Medicine 3 (UAMI 3) and Central Laboratory of the Hospital Córdoba. Voluntary participation, after signing the informed consent. As an exclusion criterion, they should not present a previous diagnosis of CD.

It was investigated in university students due to the few studies published in groups of young people and since it presented the feasibility of accessing people and facilitating the laboratory.

A filiation, demographic, and clinical data collection form was used (Table 1) with a predetermined score (major symptoms and signs and associated diseases 4 points; minor symptoms and signs 3 points; and inclusive and additional symptoms and signs without score).

Table 1 Data collection sheet

Surname and first names	**N°.**		
Age	Sex	Date	Year Entry Carreer:
Size	Weight	BMI	Country
Yes	No	Yes	N°
Diarrhea*	Asthenia	corneal ulcers	
malnutrition	Espontaneous abortions	Repetition Infect.	
Distended abdomen	arthromyalgia	Apathy	
low stature	sleep disturbances	Depression	
Rectal prolapse	seizures		
Anemia	calcified cerebral	Menarche (age)	
osteopenia	myopathies	Irreg.cycle	
Osteoporosis	infertility		
tetany	non-juvenile acne	sexual impotence	
spontaneous fractures	hipotroph musc	premat menopause	
edema	thrush	Constipation	
Alt. Dental Enamel	Incres. airborne noises	coated tongue	
Dx. previous dyspepsia	Halitosis		
type I diabetes	Dx. Previous IBS	brittle nails	
collagenopathies	Intol. Food**	Dry Skin	
Autoimmune hepatitis	Intol. lactose childhood	Fine broken hair	
thyroiditis	Intol. current lactose	early gray hair	
nephropathies	headaches	areas alopecia	
Celiac relatives	Anorexy		
Other autoimmune	Weight loss		
Physical exam			
Coagulation alterations			
meteorism-stink			
nausea-vomiting			
Recurr. abdominal pain			
low back pain			
Irritability			
conduct disorders			
*Feces characteristics			
**What foods?			
E-mail:			

Ref: Major symptoms and signs and associated diseases, highlighted in light blue. Symptoms and signs minor, highlighted in fuchsia. Inclusive symptoms and signs, highlighted in green. Symptoms and signs additional, not highlighted.

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Rutine and specific blood tests (anti-transglutaminase and anti-endomysial antibodies) were performed. The data was analyzed by adding the scores of each student's file, to which different categories corresponded with their percentages of possibilities of being celiac (Table 2).[9]

Table 2 Categories according to the score of the cards used and possibilities of being celiac, according to the index of suspicion

Category	Points	Chances of being celiac
0	0 to 7	0%
1	8 to 11	10%
2	12 to 19	20%
3	20 to 23	40%
4	24 to 31	50%
5	32 to 49	80%
6	50 +	100%

Source: Celiared Program of Argentine's Health Ministry[9]

Endoscopy and intestinal biopsy[10] (Marsh-Oberhuber classification)[11,12] were requested for students with a high level of clinical suspicion (ANSC), lacking laboratory abnormalities and/or positive antibodies. The corresponding differential diagnoses were made.

To evaluate the objective, the categorical variables were analyzed, their frequency distributions and the comparisons were made from categorized data.

A detail of the frequencies of symptoms, signs and values obtained from the laboratory was generated, they were described from their summary measures and the comparative analysis by ANAVA.

The InfoStat statistical software was used considering a significance level of 95%.

It was approved by the Research Ethics Committee of Hospital de Clínicas (UNC) and the ethical protection and confidentiality of the data recorded was maintained, which were protected according to statistical secrecy, medical secrecy and the provisions of the Argentina's National Law Nº 25326/00 (Protection of personal data).

Results

The total sample analyzed is made up of 638 students in the last years of the Medicine career (UNC).

In the distribution of the group studied according to sex, it was observed that 442 students (69.28%) were female, with a predominance over males in a ratio of 2/1 ($p<0.001$). This sample makes up 12.73% of the annual population of the carreer.

The ages ranged from 19 to 38 years, with a mean of 23.28±0.10 years. With similar values in men and women.

According to the origin, 12 students were foreigners (1.95%) and 98.5% were Argentines, from all the Argentine's provinces, except Tucumán.

The size ranged from 149cm and 197cm with a mean of 177.58±0.54cm for males and 163.37±0.32cm for the women.

The body mass index (BMI) was normal weight in 72.25% of the students (Table 3). It was followed by underweight in women and overweight in men. In all significance values the comparisons were $p<0.05$.

Table 3 Absolute and relative frequency distribution (expressed as a percentage) of the body mass index of the students according to sex. (n=609)

BMI expressed in frequency absolute and relative					
Sex	**AT and MT**	**NW**	**OW**	**OI, OII and OIII**	**Total**
Woman	41*(9.72%)	332(78.67%)	40 (9.48%)	9 (2.13%)	422
Male	2(1.07%)	108(57.75%)	65* (34.76%)	12*(6.42%)	187

Ref: BMI: designation by category of body mass index. MT: moderate thinness.

AT: acceptable thinness. NW: normal weight. OW: overweight. OI: grade 1 obesity.

OII: grade 2 obesity. OIII: grade 3 obesity. *$p<0.05$

With the scores of each file, the students were grouped into categories according to the index of suspicion with a pre-assigned possibility of being celiac (Table 2). There it was observed that the highest frequency, 542 students (85.25%), were between categories 0 and 2 (between 0 and 20% chance of being celiac), while the remaining 96 (14.75%) they were located between categories 3 and 6 ($p<0.01$), which have between 40% and 100% chances of being celiac.According to sex, it was observed that in all categories there was a predominance of women ($p<0.0001$).

The general group more frequently had between 0 and 1 major symptoms and signs (digestive, objectifiable) and associated diseases per student (Table 4) in relation to the groups with 2 or more of them ($p<0.0001$). Abdominal distension was the most frequent with 242 students (37.86%). Diarrhea occurred in 115 students (18.03%), while constipation was in 209 (32.76%). In 51 of them (8.62%) they alternated both. Changes in dental enamel occurred in 71 students (11.06%).

Table 4 Distribution of absolute and relative frequencies (expressed in percentages) of major symptoms, signs and associated diseases per student, according to sex and laboratory performed

Sx, Sg Major and associated disease				
	Women		**Male**	
N° Sx and Sg	**WOL**	**WL**	**WOL**	**WL**
0*	104 (34.35%)	49 (35%)	90 (60.26%)	20 (42.23%)
1*	100 (33.02%)	31 (22.14%)	40 (26.49%)	14 (33.33%)
2	63 (20.81%)	28 (20%)	16 (10.6%)	10 (22.22%)
3	27 (8.91%)	15 (10.72)	3 (1.99%)	0
4 to 6	9 (2.91%)	17 (12.14%)	1 (0.66%)	1 (2.22%)
TOTAL	302	140	151	45

Ref: Sx: symptoms. Sg: signs. Associated Diseases: Associated diseases. WOL: without laboratory.

WL: With laboratory. *$p<0.0001$. (n=638)

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Regarding the family presentation of CD, it was shown that 45 of all the students had at least one celiac relative (7.21%).

The students who reported edema were 41 (6.43%). Rectal prolapse manifested itself in 8 of the students (1.1%).

The minor symptoms and signs (general, extradigestive) present most frequently were between 0 and 2 per student (Table 5). Asthenia occurred in 190 students (29.78%) and recurrent abdominal pain in 183 (28.66%), followed by irritability, with 151 students (23.67%). With conduct disorders and irritability there were 153 students (23.98%).

The inclusive symptoms and signs (special risk situations) were between 0 and 1 per student and there were headaches in 279 students (44.36%), of which 222 were women (33.94%), increased airborne noises in 152 students (22.93%) and thrush in 142 students (22.57%). 58 students reported lactose intolerance (9.09%). The proportion that reported dyspepsia was 8.60% (57 students) and irritable bowel syndrome (IBS) were 64 students (9.65%), in 24 (3.76%) they were both concomitantly.

Table 5 Distribution of absolute and relative frequencies (expressed in percentages) of minor symptoms and minor signs per student, according to sex and laboratory performed

Sx, Sg MINOR				
	WOMEN		**MALE**	
N°. Sx and Sg	**WOL**	**WL**	**WOL**	**WL**
0	86 (28.81)	29 (20.71)	63 (41.73)	19 (42.24)
1	61 (20.2)	25 (17.86)	32 (21.85)	14 (31.11)
2	57 (18.54)	25 (17.86)	27 (17.88)	6 (13.33)
3	29 (9.6)	19 (13.57)	15 (9.93)	3 (6.66)
4	28 (9.27)	6 (4.29)	4 (2.65)	0
5 to 12	41 (13.58)	36 (25.71)	9 (5.96)	3 (6.66)
TOTAL	302	140	151	45

Ref: Sx: symptoms. Sg: signs. WOL: without lab. WL: With laboratory

(n=638).

86 students (10.86%) with apathy/depression were found, 22 of which had both symptoms together. Of them, 18 (7.37%) were female.

The most frequent additional symptoms and signs were dry skin in 240 students (37.46%), constipation in 209 students (32.60%), and menstrual disorders in 114 students (17.87%).

The laboratory was indicated in the total number of students, obtaining a group of 186 students with analysis carried out, representing 29.15% of the sample.

The students who reported anemia at some point in their lives were 82 (12.52%). While 19 of them (10.21%) had anemia profile by laboratory. The ionogram was altered in 44 students (23.65%). Selective IgA deficiency was present in 8 students (4.30%). The liver profile was altered in 13 students (6.99%). There were no coagulation abnormalities.

Among the students (in general) a high prevalence of symptoms and signs was detected; only 57 students (8.94%) did not have any of the symptoms of those asked (regarding CD) or laboratory abnormalities (general and specific).

When analyzing the index of suspicion of being celiac by categories among those who carried out the laboratory, it is observed that although the majority, 109 students (58.60%) had a low index of suspicion (0-10% chance of being celiac). 28 students (15.05%) had an index between 50 and 100% of possibilities of presenting the disease. Of the biopsies performed, 31.58% were normal and (68.42%) had atrophy.

After the differential diagnoses were made, 13 students (6.99%) with celiac disease were found, who presented atrophy of different degrees.

Celiacs: A female/male ratio of 2-3/1 was observed.

Among the diagnosed patients, there were no foreigners, 2 were from other provinces, 4 from the interior of the province of Córdoba, the rest were from Córdoba city.

The age distribution of the diagnosed students was21 to27 years, with a mean of 23.38±0.62 years.

The mean height was 161.50±1.14 cm, $p<0.05$ compared to non-celiacs and the mean weight was 53.50±1.32kg.

In relation to the BMI among the celiacs, 11 students, still with normal weight, were found in BMI's lower limit, while 2 of them presented an acceptable thinness. There were no overweight students among those diagnosed. Among celiacs, categories 4 and 5 with HLCS predominated, with between 50 and 80% chance of presenting the disease (9 students). Except in one case that had a 0% chance of being celiac, with few symptoms, low IgA, strongly positive antibodies, and grade IIIc biopsy.

The diagnosed students had between 3 and 4 symptoms, major signs and associated diseases per student, the most frequent was abdominal distension in 9 students (69.23%). While another 9 (69.23%) had diarrhea, 8 students had constipation (61.54%), and in 4 of them (30.77%) they alternated both.

1 student (7.69%) was found with dental enamel alterations.

6 students (46.15%) of those diagnosed had celiac relatives

Minor symptoms and signs were between 3 and 7. Recurrent abdominal pain was present in 12 students (92.31%), asthenia in 9 students (69.23%), and irritability in another 9 (69.23%).

The celiacs had between 2 and 3 inclusive symptoms and signs per student, headache was present in 8 of the celiacs (61.54%). Followed by the airborne noise increased in 6 students (46.15%). 23.8% (3 students) presented dyspepsia and another 3 (23.8%) IBS, while in 2 of them (15.38%) it was concomitant. Among the celiacs, 4 students (23.08%) presented apathy/depression and only 1 (7.69%) was concomitant. With conduct disorders there were 4 students (30.77).

2 students (15.38%) had oral thrush, 4 had edema (30.77%). Lactose intolerance manifested itself in 5 of them (38.46%). Comparatively evaluating the age at menarche between the students in the celiac group and the non-celiac group, no significant differences were observed.

The number of students with altered specific laboratory is observed in Table 6. 61.54% (8 students) of the diagnosed group had negative antibodies.

Selective IgA deficiency was observed in 8 students (61.54%).

Discussion

CD is a major and growing public health problem worldwide because it affects children and adults, both in developed and not developing countries, presenting serious complications and sequelae that are even life-threatening and has negative economic consequences.[13]

Table 6 Distribution of the number of students with the specific laboratory altered (n=186)

Lab. Spec. altered	AF		
	Woman	Male	Total
Total IgA	7	1	8
IgA PGD	1	0	1
IgA EMA	3	0	3
IgA TTG	3	0	3
IgG DPG	3	0	3
Total Lab.	141	45	186

Ref: Specific Lab: specific laboratory. AF: absolut frecuency. IgA EMA: IgA anti-endomysial. IgA TTG: IgA anti-transglutaminase. IgA DPG: IgA anti-deaminated gliadin peptide.

Total Lab: total of students who completed the laboratory

It is the most frequent chronic autoimmune enteropathy in the world today and one of the most frequent genetically transmitted diseases in mankind. It is an emerging pathology of universal distribution.[8]

The proportion of known CD cases, in relation to those not diagnosed, is between 3 and 10% for Collin[14] and between 1 and 7% for Catassi[15] and Vavricka[16] showing that CD is clearly under-estimated and under-diagnosed.

CD has a multiform clinical expression with a spectrum that varies from the classic form with gastrointestinal symptoms to the atypical forms with extraintestinal, oligosymptomatic symptoms or silent symptoms.[17] The longer the celiac intestine is in contact with gluten, The more chance it has to suffer serious complications and other autoimmune pathologies.[15] Based on the above, the importance of early diagnosis can be visualized. GFD produces the disappearance of signs and symptoms and recovery of quality of life.[18] In children, the intestine (if the GFD is strict) cures 100%, this percentage decreases in adults.[19]

The distribution of students according to sex coincides with the data referenced in the UNC Medicine carree and consistent with the feminization of the enrollment observed in other UNC health faculties[20] and other universities in the country, Latin America and Europe.[21]

The female/male ratio coincided with the majority of authors.[22]

The age distribution agreed with the young adult for the WHO, since it was a study based on a convenience sample of university students.

In relation to origin, both the proportion of foreigners and Argentine students was similar to that reported in the 2021 UNC Yearbook with respect to the total population of the Medicine carreer.[20]

Among the clinical characteristics it was observed in the same way thatSchøslera higher percentage of these patients are underweight.[23] Dewar states that there are 30% of patients who are overweight and obese, who would be within the group of undiagnosed celiacs.[24] Therefore, being overweight should not be a reason to lower the suspicion threshold for this pathology.[23,25]

The prevalence of celiac relatives is similar to that found by authors such as, Casellas[26] Meseeha[27] and Chiu[28,29]

In this group of young adults, extraintestinal symptoms were found mostly, corresponding to atypical celiac disease, coinciding with Vivas and other authors.[30]

Abdominal distension was one of the major gastrointestinal symptoms (classic celiac disease) higher than that found by Casellas, who refers to it as the symptom that led them to the consultation.[26] Polanco expresses that it is the most frequent even in those "silent" patients.[6] Diarrhea followed, According to Pulido, in 5,912 adults, diarrhea was one of the symptoms that occurred most frequently in the consultation prior to the diagnosis of CD.[31] Volta found 13% constipation among celiacs.[32] For Polanco, coinciding with the present work, constipation occurs more frequently in adults[6] than in children, in some cases, constipation and diarrhea alternate, which is often confused with IBS.[33]

Dental enamel alterations, such as hypoplasia, are a frequent sign among celiacs,[7,34] it was higher than that found by Bottaro of 1.3%;[35] Oliveira observed it in 2.5% of children with CD and may be the only symptom at the time of diagnosis.[36]

When studying the minor symptoms, asthenia was the most frequent in line with the percentage of Pulido, which was 74.2%[31] and unlike Casellas, which was 38.3% among patients with celiac disease.[26] It was followed by irritability, which for Smith the majority decreases with GFD.[37]

Recurrent abdominal pain is a frequent reason for consultation in primary care, with high healthcare costs,[30] for Al Hussaini it was the most frequent symptom with 25.6% in the general group compared to 35.3% in those diagnosed.[38,39]

Osteoporosis is a sign with important repercussions in the life of the celiac that can even lead to spontaneous fractures.[40,41] Only students with mild bone pain consistent with their age were found. Vilppula found osteopenia and osteoporosis in 22 of 35 new positive biopsies from the adult population.[42]

Among the inclusive symptoms, headache was the most frequent. Lower was the proportion found by Benjilali, 12% of the population had migraines and 28% among celiacs, the majority improved with the gluten-free diet (GFD) as well as other symptoms.[43,44]

The proportion that reported dyspepsia was consistent with Kelly et al.,[13] IBS may be concealing an undiagnosed CD, the overlapping of symptoms between the two is evident, which delays the diagnosis. Aziz, in a group of 5,300 patients with IBS, found 4.7% of celiacs confirmed by biopsy.[45] The psychiatric disorders most frequently associated with CD are behavioral changes, short-term memory loss, anxiety, depression, sleep disorders, cognitive impairment, psychosis, and attention deficit disorders.[46] In the group of celiacs by Bottaro. Neuropsychiatric alterations were present in 2.2%.[35] In the general group, 10.86% of students with apathy/depression were found, of which 4.39% were concomitant. Of them, 7.37% were female. Among celiacs, 23.08% presented apathy/depression and only 7.69% was concomitant. Other authors report depression in up to 80% of patients and only a third improve with GFD.[28,47,48,49] It occurs in both men and women with celiac disease,[50] Gudrun.

They found a greater risk of psychiatric disorders (apathy and depression more frequently), which could be explained by tryptophan malabsorption that leads to decreased serotonin and cytokine synthesis. Their study also includes an increase in these adolescent and young adult patients with anorexia nervosa and bulimia (pathologies that were not considered in this work).[51] According to Simsek publication, patients who strictly follow the GFD have a significant decrease in depression levels compared to celiac patients who do not adopt this diet.[52] Sainsbury reports that post-diagnosis depression negatively influences adherence to the GFD.[53] For Claire,

6.7% of all adults were clinically depressed; this represents 3 times more than the general population in the United States of America.[50] Anxiety, depression, and fatigue are common complaints in patients with untreated CD and contribute to decreased quality of life. With conduct disorders and irritability there were 23.98% of which 19.59% were women. Among the celiacs, 69.23% presented irritability and 30.77% behavioral disorders, all of the latter were concomitant with irritability. Although some aspects of these conditions may improve within a few months after starting a GFD, other patients continue with significant psychological morbidity.

A systematic search for celiac disease is suggested in all patients presenting with epilepsy or with complex neuropsychiatric conditions and brain calcifications, since early initiation of a gluten-free diet can improve prognosis.[54] Oral thrush is also very common among celiacs and dentists are the ones who refer them for study.[55] In a recent study, Krzywicka demonstrated that oral thrush and mucosal ulcerations are frequently associated with children and adolescents with undiagnosed CD.[56]

Those who reported edema were above the figures reported by Bottaro of 0.6% of his patients.[35]

It is not frequent to find rectal prolapse in adults. Unlike Errázuriz, who show 2 cases of children with the presence of rectal prolapse at the time of diagnosis.[57]

Among the additional symptoms, it is common to find alterations in the menstrual cycle and, among them, menarche, which is considered by the WHO as late after the age of 14.[58] There was no significant difference between the ages of menarche of the students in the general group and those with celiac disease. Neither did they report amenorrea.[59] Probably due to the age of the group, no spontaneous abortions or early menopause were found, both frequent symptoms in celiac patients. Neither did they refer female or male sexual impotence.

The students who reported anemia agree with Kelly and Lasa.[13,60] and for Pivetta and Greenaway, all patients with non-hemorrhagic anemia should undergo a duodenal biopsy.[61,62]

A quarter of the children studied by Sharma had coagulopathies at the time of diagnosis, which reversed with the administration of vitamin K.[63] Although it is frequent, in the group studied there were no coagulation disorders. Those who reported lactose intolerance are above the percentage estimated by Chiu, for whom untreated celiacs are 4.30% more likely to suffer from lactose intolerance than the general population.[28]

For Polanco, patients with negative antibodies and positive HLCS criteria (these frequently occur in this work) should undergo endoscopy and duodenal biopsy.[5,6,16,64]

Among the laboratory alterations, only phosphorus was altered in the ionogram. Oliveira recommends the detection of CD, especially in the presence of hipocalcemia.[19,65] Although there was no hypertransaminasemia[66] among celiacs; according to Kwiatek, with DLG they normalized their enzymes within a year.[67]

Selective IgA deficiency has an incidence ten times higher among celiacs than in the general population and is in agreement with the findings of this work.[16,68]

The lower clinical, analytical and histological expressiveness in adult forms makes its diagnosis more complex than in pediatrics.[16,30] In the intestinal biopsy, the degree of histological lesions is inversely correlated with age. Therefore, with increasing age, antibody titers decrease and histological damage is less marked. According to Vivas, this lower clinical, analytical and histological expressiveness in adult forms delays its diagnosis and makes it more complex than in pediatric forms.[30]

According to Polanco, refractory CD is non-existent in the pediatric age group and, although infrequent in adulthood, it is related to a late diagnosis or a lack of adherence to the GFD.[6]

The diagnosed cases of CD in Argentina only represent "the tip of the iceberg", as is estimated in the rest of the world.[69,70] Therefore, it is important to investigate this pathology among those patients with HLCS criteria or with pathologies at risk of developing the disease, such as first- and second-degree relatives of celiac patients, type 1 diabetics, IBS, autoimmune thyroiditis, and other autoimmune pathologies that often they are triggered first.[29]

Different studies show how the prevalence has been increasing in recent years, ranging between 0.40-3%,[23] as a consequence of various factors such as more extensive information on the disease, improvements in diagnostic techniques, infant eating habits and even changes in the intestinal microbiota.[71] For Choung between 18 and 39 years of age there are 3% of undiagnosed celiacs[72] and there are no differences between men and women.[73] It is noteworthy that in the group diagnosed, many of them did not present positive antibodies, in the bibliography it was found that the data in terms of their specificity and sensitivity in adults, are disparate.[4,16] In some cases it may be due to decreased total IgA, in others to the fact that the atrophy is grade II or II-III.[28]

The Prague Consensus (2016) concluded that biopsy continues to be the gold standard for adult diagnosis.[74,75] In the investigated group, there were no students with questionable biopsies. In this case, the genetic detection of HLA DQ2/DQ8 and its alleles can be added, an index of CD predisposition that has a high negative predictive value, and a low positive predictive value.[76]

Although the real value of a screening program seems obvious, not all authors are in favor of this strategy.[77]

Mass screening for celiac disease meets most of the criteria set forth for a mass medical review by Wilson and Jungner adapted by the WHO.[78]

It is a common disorder with significant morbidity and mortality.

Early detection is difficult based on clinical data.

If it is not recognized, it can manifest itself with severe complications.

There is an effective treatment (GFD).

Non-invasive, sensitive, specific and simple serological tests are available for screening.[16,79]

In accordance with the above criteria, the WHO could endorse screening in the entire population.[16,79] In many cases, the Cost-effectiveness of a screening in the adult population would be justified.

A high percentage of celiacs, 6.99 % (13 students), was found in this work. It is important to know that most authors agree that the percentage of known cases worldwide is only the tip of the iceberg. The cases that have not been diagnosed are between 3 and 10% according to different authors[14,15,16] and would be represented by the ice that is below the water line in the celiac iceberg. This paper shows that if the disease is properly investigated it can reach a much higher prevalence.

This work was carried out on young adults, "supposedly healthy" but with many symptoms that the patient seems to minimize.[79,80]

It is under discussion whether screening for CD should be performed, in whom it should be done, at what age and what would

be the antibodies to recommend.According to Polanco, in adolescence it is rare for the disease to present with a clinical form of classic presentation and this delays the diagnosis.[60]

While doctors think about what type of screening to do (general population or risk groups, at what age and other variables), these undiagnosed celiacs begin to present associated diseases[81] such as anemia, osteoporosis, sterility, type I diabetes, thyroiditis, other autoimmune diseases and their irreversible complications.[5] When the diagnosis is made in the child, the shorter contact time of the intestine with gluten means that other pathologies do not appear and until their height increases, their intestine recovers 100%, not so when the diagnosis is made in the adult.[6,82] For Mennini, It is important that screening also starts at an age in which GFD can be implemented in a monitored environment (home/school), being more easily accepted and ensuring that patients are monitored after diagnosis.[83] Then, the true objective would be not only a new diagnosis but a useful diagnosis.[82] Based on the above, the importance of early diagnosis can be visualized.[3,6]

It is worth asking whether it is ethical to talk about cost/benefit[84] when an undiagnosed patient can evolve into a malignant disease. It is indisputable that health should be a right for all. The HLCS can be useful in the first stage of screening and the specific antibodies (non-invasive study), occupy the second step, before performing endoscopy and biopsy. The undiagnosed celiac is demanding medical assistance either in the public or private sector with an increase of approximately 40% of the cost.[65] Countries like San Marino test their entire population, although in this study the percentage is out of date and is only in children, with 2% celiac disease.[85] Mexico shows 2.88% in a sample of blood donors,[86] Uruguay has 4 to 12% among 1st and 2nd relatives of celiacs.[82] Chile presents 1.7% asymptomatic.[69] Brazil 4.5%, Venezuela 3%.[87] In Misiones, Argentina, there is a study with 4.4% of celiacs in the Toba indigenous population.[88] These are the few studies carried out in Argentina and Latin America.

After around 4 years of strict GFD, morbidity and mortality is reduced regardless of age and sex.[89] And recovers the quality of life.[90]

According to the prevalence of 1% of the population (1,330,000 inhabitants according to the 2010 national census) (data from the 2022 census are not yet available), the number of celiacs in Córdoba Capital[91] is estimated at 13,300 . Those not diagnosed (in a ratio of 7/1) would be around 93,100 that should be detected before serious complications occur.[15]

The potential or strength of this study lies in the fact that it warns about the need to systematically study the possibility of the presence of CD in those who have the clinical profile of these students (HLCS). The diversity of both digestive and extra-digestive symptoms makes diagnosis difficult and delayed. And theseUndiagnosed patients remain at risk of serious, irreversible complications and other autoimmune diseases.

And its weakness is that not all those who presented HLCS continued with the study sequence.

For all of the above, early diagnosis is very important.[3,6]

Conclusion

In a population of 186 “healthy” asymptomatic students who carried out the laboratory, a high percentage of celiacs was found 6.99%, 13 students figure higher than 1-2% referred to as prevalence in the general population. CD is highly prevalent with a heterogeneous clinical presentation that is under-estimated and under-diagnosed in general throughout the world and particularly in the group studied. These values alert to the need to systematically study the presence of CD in those with this clinical profile.

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Conflicts of interest

The authors declare that there is no conflict of interest.

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