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Clinical profile of Brazilian patients aged over 50 years at the diagnosis of celiac disease

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INTRODUCTION

Celiac disease (CD) is a multisystemic complex immune-mediated disorder (IMD), which is triggered and maintained by gluten in genetically susceptible individuals. Despite the availability of autoantibodies as CD biomarkers and upper endoscopy facilities with duodenal biopsies, most patients with this disorder remain undiagnosed[1]. CD is traditionally diagnosed in children and adolescents. However, some authors reported higher detection in the elderly population[1,2] and that about 25% of celiac patients were first diagnosed in the seventh decade in countries such as Canada, the United States, and Northern Europe[2].

The heterogeneous mode of clinical presentation, with digestive and extra-digestive manifestations, might be responsible for the delay in the diagnosis, besides the poor awareness by primary care providers or specialists without a high index of suspicion[2-4]. The physician should consider the diagnosis, order the correct tests, interpret them, and know when to refer the patient to a gastroenterologist expert in CD. As the CD prevalence in adults occurs in the third and fourth decades of life, patients aged above 50 years can be misdiagnosed with great delay and repercussions in their quality of life (QoL)[1,3,4].

This study aimed to evaluate the clinical profile of Brazilian patients aged over 50 years at the diagnosis of CD.

METHODS

This study was approved by the Ethics Committee of the Evangelical Beneficent Society of Curitiba under protocol CAAE 84793318.0.0000.0103. This is a retrospective study conducted through a review of clinical charts. The same physician attended to all patients in a single private practice in the city of Curitiba, Brazil, from 2010 to 2020.

Patients aged 50 years or more diagnosed with CD[5] were included in this study. A structured questionnaire was used, comprising questions about complaints related to the digestive tract and other systems. Cases with incomplete data were excluded.

The symptoms of the digestive and extra-digestive tract were based on the transcriptions of patients' subjective reports. Gastrointestinal (GI) symptoms, such as aphtha, gastroesophageal reflux, epigastric pain, bloating, indigestion, nausea, vomiting, flatulence, abdominal pain, diarrhea, and constipation, were investigated. Personal comorbidities before this investigation and information regarding drugs currently being used were obtained.

Routine laboratory tests were required. DEXA (dual-energy X-ray absorptiometry) was conducted for bone disease evaluation[6].

Data on upper endoscopy were collected on all patients, with gastric biopsies performed in cases with macroscopic alterations. Duodenal biopsies were performed based on the recommendations: one or two fragments of the bulb[7], and four to five specimens from the second portion of the duodenum and classified according to Marsh[8,9].

Statistical analysis

The data were tabulated and expressed as median and interquartile ranges (IQR), mean and standard deviations, or frequencies and percentages.

RESULTS

A total of 40 Caucasian patients, 34 (85.0%) female and 6 male, with a median age of 59.5 years were studied (IQR=50–79 years).

Table 1 shows the digestive manifestations in the study patients, with no gender differences. Flatulence and bloating were the more frequent complaints.

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Table 1. Digestive symptoms and signs referred by the study patients (n=40).

Symptoms	Total n (%)
Flatulence	35 (87.5)
Bloating	30 (75)
Esophageal reflux	21 (52.5)
Diarrhea	21 (52.5)
Aphtha	16 (40)
Epigastric pain	16 (40)
Abdominal pain	16 (40)
Nausea	14 (35)
Maldigestion	14 (35)
Constipation	9 (22.5)
Vomit	7 (17.5)

Anemia was observed in 37 (32.4%) patients, with iron deficiency in 12 (34.3%) patients and vitamin B12 deficiency in 7 (20.6%) of the cases. Vitamin D levels decreased in 89.3% of the cases. DEXA was performed in 32 cases, with 53.1% of osteopenia and 37.5% of osteoporosis detected in the femur, and 25.9% of osteopenia and 28.1% of osteoporosis detected in the spinal cord.

Patients mentioned non-drugs that could alter the histological findings at the time of consultation.

Table 2 presents extra-digestive manifestations that can occur alone or along with GI symptoms. Psychiatry diseases were the most frequent, affecting 87.1% of the study patients.

Out of 40 patients, 39 (97.5%) reported at least one IMD before the diagnosis of CD, being autoimmune hypothyroidism observed in 14 (35.9%) and Sjogren's syndrome in 2 (5.1%). IMDs, such as hyperthyroidism, Behçet's disease, type 1 diabetes mellitus, macroamylasemia, lupus erythematosus, juvenile rheumatoid arthritis, scleroderma, vasculitis, multiple sclerosis, common variable immunodeficiency, and asthma, were reported in one patient each.

Table 3 displays the upper endoscopic, ileocolonoscopic, and histological findings in the study patients. Marsh III was observed in 72.5% of patients.

DISCUSSION

Despite the obvious tolerance to gluten ingestion, as emphasized by Beaumont and Mian since 1998, CD is increasingly being identified in later life[10]. There are few epidemiological studies on middle-aged and older patients, mainly in Brazil. CD in this population has been underdiagnosed due to the lack of physicians' awareness of CD occurrence in this age

Table 2. Complaints and main previous comorbidities referred by the study patients (n=40).

Comorbities	Total n (%)
Psychiatric	
Anxiety	20 (51.3)
Depression	14 (35.9)
Musculoskeletal	
Arthralgias	10 (25.0)
Fractures	7 (17.9)
Neurological	
Migraine	7 (17.9)
Headache	3 (7.5)
Insomnia	4 (10.2)
Cutaneous/mucosal	
Dermatitis herpetiformis	4 (10.2)
Oral lichen planus	2 (5.1)
Cardiovascular	
Arterial hypertension	7 (17.5)
Respiratory	
Respiratory allergy	5 (12.5)
Endocrinological	
Hypothiroidism	14 (35.0)
Pancreatic insufficiency	2 (5.1)

Table 3. Upper endoscopic and histological findings in the study patients.

Gastrointestinal segment	n (%)
Esophagus	
Macroscopy	
Normal	25/40 (62.5)
Esophagitis	14/40 (35.0)
Hiatal hernia	1/40 (2.5)
Stomach	
Macroscopy	
Normal	16/40 (40.0)
Gastritis	23/40 (57.5)
Gastric atrophy	1/40 (2.5)
Microscopy	
Normal	6/14 (42.8)
Gastritis	12/22 (54.5)
Lymphocytic gastritis	2/14 (14.3)
Duodenum	
Macroscopy	
Normal	10/40 (25.0)
Alterations	30/40 (75.0)
Microscopy*	
Normal	0
Marsh I	2/40 (5)
Marsh II	9/40 (22.5)

*Marsh classification – Reference 9.

group and the heterogeneity of clinical presentation[2,11]. Their subtle or atypical symptoms may go undetected by healthcare professionals, and the delay in CD diagnosis can lead these patients to consume gluten for extended periods[12]. The CD diagnosis in older patients follows the same guidelines as in young people. However, the clinical diversity and the lower frequency or intensity of symptoms than seen in children or adolescents frequently delay and obscure the CD diagnosis, in particular in patients aged over 50 years, as it is easy to dismiss such symptoms due to "old age"[2,13]. The GI complaints referred by our patients were similar to those reported in young Brazilian adults by Lima et al., in both genders[14] and to Italian and Finland studies[1,15].

In our data, extra-digestive manifestations were highly frequent and reinforce that patients aged over 50 years had symptoms related to all other systems and could be attended to by specialists that cannot be aware of CD as the basic disorder[1,3,4].

In our study, psychiatric and neurological symptoms, which are common in this age group, could be part of the CD spectrum of manifestations, similar to those described by other authors[16,17]

The risk of complications is higher in patients with late recognition of CD because gluten testing is more time-consuming[2]. We observed that anemia and bone disorders were more frequent. Anemia by iron deficiency or vitamin B12 deficiency was detected in one-third of the cases and is similar to that observed in adults from the same geographical area[14]. Regarding bone disorders, we detected osteopenia in the femur (53.1%) and osteoporosis in the spinal cord (28.1%), which is consistent with other studies[1]. Low bone mineral density (BMD) is a common finding in Brazilian patients with CD, as described previously by the same research group, studying CD patients and healthy controls with similar age, ethnicity, and geographical area[17,18]. Identifying low BMD is crucial to allow calcium and vitamin D supplementation and reduce the risk of fracture[19].

We observed several IMDs affecting celiac patients, the most common of which is hypothyroidism. Common inflammatory pathways, similar genetic factors, environmental triggers, and pathophysiological mechanisms were reported[20]. Furthermore, female gender, age at diagnosis, and family history positive for IMDs are recognized risk factors[21]. In our study, at least one IMD had affected practically all patients (39 out of 40). Elli et al., reported a higher prevalence of IMDs in patients with CD compared to the general population (23 vs. 0.4%)[21] in Italy, which is similar to that reported by Castro et al., in Ireland (31.1%)[22]. This study, as proposed by Elli et al., implies that patients with CD should also be examined for other IMDs[21].

At upper endoscopy, in this research, normal mucosa of the esophagus was observed in two-thirds of the cases and non-erosive esophagitis in one-third of the cases. Routine biopsies are not recommended[23], which have no direct correlation with the complaints of gastroesophageal reflux[24]. Studies reporting the association between CD and gastric disorders indicated conflicting results[24,25], and there are controversies if gastric biopsies should be routinely taken during upper endoscopy in CD patients[26].

Duodenal biopsies were performed to confirm CD diagnosis in patients ingesting gluten. Complications are unusual after duodenal biopsies even among the elderly patients[27]. According to the Marsh classification[9], two-thirds of the patients presented Marsh III. Ciccocioppo et al., after comparing duodenal lesions, reported 86% of Marsh III in childhood vs. 51% in adulthood[28]. Nonetheless, duodenal biopsy remains an important component in the diagnosis of adult patients with suspected CD[3,4].

This study was limited by its retrospective approach and small sample size. However, since all patients were attended to by the same physician, the same clinical and laboratory protocol was applied. Also, the same pathologist analyzed the biopsies, reducing the bias.

Interestingly, some people can consume gluten for 50 years before developing CD, while others consume gluten for only 9 months before being diagnosed. However, why to wait for end-stage celiac disease to occur when it can be prevented by early diagnosis? Early diagnosis and CD treatment can prevent complications in these people[29].

In conclusion, our patients diagnosed with CD after 50 years of age had a significant prevalence of IMDs before the diagnosis, as did their family members. Most patients manifested classical CD symptoms and total duodenal atrophy, revealing the severity and difficulty in nutrient absorption.

ETHICS APPROVAL

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. This study was approved by the Committee of Ethics in Research of Faculdade Evangélica Mackenzie de Medicina, Curitiba, PR, Brazil, which can be contacted by telephone number +55 (41) 3240-5570 or by e-mail at comite.etica@fempar.edu.br.

AUTHORS' CONTRIBUTIONS

LMSK: Conceptualization, Data curation, Formal Analysis, Methodology, Writing – original draft, Writing – review

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