



Review Article

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Prevalence of Carcinoma in Celiac Patients



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Abstract

Celiac disease (CD) is an autoimmune disease that affects genetically predisposed individuals. The prevalence among people of European descent is about 1%, and it is estimated that in Brazil about 300 thousand people have the disease. The celiac is subject to several mild complications, such as diarrhea, flatulence and abdominal distension. However, those who are not diagnosed or who do not adhere to the gluten-free diet are prone to develop malignant complications such as cancer. Celiacs are 1.29 times more likely to develop intestinal and extra-intestinal neoplasms than healthy people and are more likely to develop non-Hodgkin's lymphoma and small bowel adenocarcinoma.

Keywords: Celiac disease; carcinoma; prevalence; complications

Abbreviations: CD: Celiac Disease; NHL: Non-Hodgkin's; LPD: Lympho-Proliferative Disorders

Introduction

Celiac disease (CD) is an autoimmune disease that affects genetically predisposed individuals through the ingestion of foods containing gluten proteins, the main compound of wheat, oats, rye, barley and malt [1-3]. It is characterized by changes in the small intestine of the carriers, such as the decrease of the intestinal villi and, consequently, of the area of nutrient absorption [3,4]. The prevalence of the disease among people of European descent ranges from 0.3 to 1% [1,5-7]. In Brazil, official statistical data are unknown, however, it is estimated that 300,000 Brazilians are carriers of the disease [1].

The celiac is subject to several mild complications, such as diarrhea, flatulence and abdominal distension; however, in some cases, there are reports of severe respiratory, neurological, nutritional, obstetric and reproductive complications, in addition to mainly several types of neoplasias that raise mortality rates [8-10]. Patients, especially those not diagnosed or who do not adhere to the gluten-free diet, are likely to develop malignant complications, such as cancer [11], and it has been reported that the main celiac carcinomas are lymphomas and adenocarcinomas [12]. Given the severity of the correlation between carcinoma and celiac disease, this article aims to review the prevalence of major cancers associated with celiac disease.

Types of Carcinoma and Prevalence

Celiacs are 1.29 times more likely to develop intestinal and extra-intestinal neoplasms than healthy people [13,14]. Celiac

patients are primarily affected with non-Hodgkin's lymphoma and small bowel adenocarcinoma [14-16], however, there are other types of carcinomas such as oesophageal and oropharyngeal reported but are less frequent, but the consequences are equally severe when untreated [17-19].

Lymphomas are neoplasms characterized by the transformation of any class of lymphocytes into malignant cells. Most of them originate from lymph nodes or ganglia. There are two classes of lymphoma. Hodgkin's disease, characterized by the presence of large cells called Reed-Sternberg, and inflammatory cells. This class represents 12% of all cases. Unlike the first subtype, non-Hodgkin's (NHL) is much more common, being subdivided into NHL T lymphocytes, which encompass cutaneous T cells, peripheral T cells and T-cell lymphoma associated with enteropathy, and NHL B cells encompass lymphoma Diffuse large B-cells, mantle cells, marginal and follicular zone [20].

Although it is less frequent than the subtype that affects B-cells, T-cell lymphoma when associated with the disease is the leading cause of death in patients, and usually, develops in the jejunum, however, it may occur in the ileum and extra intestinal sites, such as liver, brain, chest and bone [21]. This type of carcinoma is most prevalent in people close to 60 years of age and the survival rate is relatively low, about 15-20% of patients survive up to 2 years [20].

In a study by Catassi et al. [21] in a group of 653 patients with lymphoma 6 celiacs (0.92%) were identified, of which 3

were B-cell lymphomas and 3 T-cell lymphomas. Most of these cases reported the disease was mainly in the intestine [22]. Leslie et al. [20] studied 1,285 patients with biopsy proven celiac disease during the years 1981 and 2010 and identified 40 cases of lymphoma, of which 33 were non-Hodgkin's lymphomas. Among these identified cases, 16 were characterized as B-cell NHL, another 12 cases were NHL T lymphocytes associated with enteropathy and another 5 were NHL T cells not associated with enteropathy. Patients who developed lymphoproliferative disorders (LPD) were older in the diagnosis of celiac disease (57.9 ± 15.5 vs 42.5 ± 17.4 years, $P < 0.0001$) and more likely to present diarrhea (60, 0% vs. 39.8% $P = 0.016$), abdominal pain (17.5% vs. 5.5% $P = 0.0046$), and / or weight loss (12.5% vs. 4.0% $P = 0.028$). Patients with enteropathy-associated T-cell NHL had a shorter mean survival than patients with non-enteropathic T-cell NHL (3.2 versus 15.0 years, $P = 0.016$) [20].

In addition to lymphomas, there is also a high risk of adenocarcinomas of the oropharynx, oesophagus, pancreatic, hepatobiliary and mainly intestine [2,3,23]. Adenocarcinoma is a malignant neoplasm that occurs in glandular epithelial tissues, which are generally extremely aggressive and difficult to remove surgically, which results in an unfavorable prognosis; however, if removal occurs, the prognosis is better than patients with lymphoma [24-26]. Its incidence under normal conditions is approximately 1 case per 100,000 people, representing about 5% of all cancers of the gastrointestinal tract [27-29]. Experts suggest that adenocarcinomas associated with celiac disease have arisen through the development of an adenoma for carcinoma [11,28]. Although less frequent than lymphomas, Freeman et al. [23] identified in a group of 35 patients with celiac disease reported after 60 years, 10 cases of lymphoma and adenocarcinoma of the small intestine [23]. Howder et al. [16] conducted a study of 395 reported cases of carcinomas in the UK and found celiac disease associated with 39% of lymphomas in a group of 107 patients and 13% of small bowel adenocarcinomas in a group of 175 patients [16].

An increased risk of oesophageal and pharyngeal carcinoma has been reported [17,18,26]. In a study conducted by Askling et al. [30] a population cohort with 11,019 celiac individuals was used. The incidence analysis in this cohort showed a 2.3-fold increased risk of celiac disease developing oropharyngeal cancer and a 4.2-fold increased risk of oesophageal cancer [30]. However, these results have not yet been replicated in American countries.

Conclusion

Due to the immunogenic characteristic of the celiac disease and the persistence of not implementing a strict gluten-free diet, patients are increasingly likely to develop a range of malignancies whose survival time is sometimes unsatisfactory. Reports of previous studies by several authors show the prevalence of neoplasias and their complications. These studies

reinforce the high degree of dangerousness of celiac patients, as well as the need for a rigorous dietary implementation and the development of new treatment approaches.

Competing Interests

None of the authors has any competing interests.

All authors contributed equally to this work.

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