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ORIGINAL ARTICLE

# Celiac Disease: Similar Presentations in the Elderly and Young Adults

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**Abstract**

*Background/Aims* Studies have shown that celiac disease can affect individuals in all age groups. However, few studies have described the disease in the elderly. The goal of this study is to characterize celiac disease in the elderly by comparing to a population of young adults with celiac disease.

*Methods* Review of a tertiary center database of patients with celiac disease was performed to identify two groups of patients, an elderly cohort ≥65 years and a young adult cohort aged 18–30 years, with biopsy-confirmed celiac disease. Information obtained included symptom duration, clinical presentation, small intestinal pathology, associated conditions, and the presence of bone disease.

*Results* Included in the study were 149 young adult and 125 elderly patients; the latter represented 12.4% of the patients in our database. The duration of symptoms prior to diagnosis was similar, 5.8 ± 12 years and 6.14 ± 12.6 years in the young adult and elderly cohorts, respectively ($p = 0.119$). There was no significant difference in the mode of presentation of illness. Diarrhea was the main presenting symptom (49% in young adults vs. 50% in the elderly, $p = 0.921$). There was a similar prevalence of autoimmune disease (19% in young adults vs. 26% in the elderly, $p = 0.133$). Thyroid disease and neuropathy were more prevalent in the elderly ($p = 0.037$ and $p = 0.023$, respectively). The degree of villous atrophy and prevalence of bone disease were similar in each group.

*Conclusions* Surprisingly, the presentation of celiac disease both clinically and histologically is similar in elderly and young adult patients. The factors triggering disease at any given age remain unclear and warrant further study.

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**Keywords** Celiac disease · Elderly · Villous atrophy · Bone disease

## Introduction

Celiac disease is an autoimmune enteropathy with multisystem involvement triggered by the ingestion of gluten and other related proteins in genetically predisposed individuals [1]. It is a common disorder affecting up to 1% of the general population, [2, 3] and has been described primarily in children and young adults. The clinical presentation can be variable, ranging from classic symptoms of malabsorption, commonly seen in children, to more subtle findings typically seen in adults [4]. Intestinal symptoms have been reported to be less prominent in elderly celiac patients who may present with only nutritional deficiencies [5]. Celiac disease often co-exists with autoimmune diseases such as insulin-dependent diabetes, autoimmune thyroiditis, and Sjögren's syndrome [6, 7].

Among adults, the peak age of diagnosis is between 40 and 60 years, and women constitute the majority of adult cases [8]. Data suggest that the incidence of celiac disease is increasing in the adult population, particularly among the elderly. Recent studies report that the incidence ranges from 19% to 34% in this age group [9, 10]. Data from Murray et al. [8] suggest that the incidence rates are continuing to rise in the elderly. Moreover, it has been shown that celiac disease may actually develop de novo in elderly patients [11].

To date, there are no studies that have compared the characteristics of celiac disease in the elderly with young adults. The goal of our paper is to analyze a large cohort of patients from a similar geographic region treated at a university-based celiac disease center in the US to compare clinical and histological features of celiac disease in the elderly with a population of young adults.

## Materials and Methods

Clinical data of all patients with celiac disease ($n = 1{,}008$) were reviewed from a prospectively generated database at a university-based referral center. We only included patients who had biopsy conformation of the diagnosis. Patients were divided into two cohorts: young adults aged 18–30 years and elderly patients diagnosed at $\geq$65 years. Both groups were derived from similar geographic locales. Data from each patient group were analyzed for various clinical features of celiac disease. These features included mode of presentation of illness such as diarrhea, anemia, bone disease, screening, incidental diagnosis during endoscopy, abdominal pain, weight loss, and chronic fatigue. Other clinical factors that were analyzed included duration of symptoms prior to diagnosis and presence of associated diseases including dermatitis herpetiformis, neuropathy, and autoimmune conditions.

We also assessed for bone disease in patients who had dual-energy x-ray absorptiometry scans (DEXA) within 1 year of diagnosis. We compared the mean bone mineral density (BMD) of patients with celiac disease to age and gender-matched values reported by one DEXA equipment manufacturer (Hologic Corporation, Bedford, MA) by calculating the *T*-score (deviations from sex-specific peak bone mass in standardized units) and *Z*-score (deviations from sex-specific and age-matched peak bone mass in standardized units). Both the *T*-score and *Z*-score are normally distributed with a population expected mean of 0.00 and a standard deviation of 1.00. We calculated *T*-scores and *Z*-scores at the hip to classify patients with osteopenia or osteoporosis.

Other data collected for each patient included small-intestinal biopsies that were reviewed and scored using the modified Marsh criteria [12, 13]. In the young adult cohort, there were 114 patients and in the elderly group there were 100 patients who had pathology available for review.

Patients were excluded if they did not meet age criteria or lacked biopsy data consistent with a diagnosis of celiac disease.

The data were analyzed using *t*-tests and Mann–Whitney rank sum tests to compare the two cohorts and determine whether observed differences achieved statistical significance. This study was approved by the institutional review board.

## Results

### Demographics

We identified 125 patients who were diagnosed at age $\geq$65 years and 149 patients diagnosed between the ages of 18–30 years, comprising 12.4% and 14.8% of the study population, respectively. There was a predominance of females in both groups. This finding was less marked in the elderly population, F:M—1.3:1 in the elderly cohort compared to 3.8:1 in the young adults ($p < 0.001$; Table 1). The mean age at diagnosis of celiac disease in the elderly cohort was 71.7 ± 4.4 years. The duration of illness prior to diagnosis was similar in each age group, 5.8 ± 12.0 years in the young adult group and 6.1 ± 12.6 years in the elderly cohort, ($p = 0.119$).

### Presentation of Illness

The mode of presentation of celiac disease in our study is shown in Table 2. The majority of patients in both groups presented with the classic symptom of diarrhea, 50% in the

**Table 1** Demographics of study population

| Demographics | Age 18–30 years No. (%) | Age ≥65 years No. (%) | *p*-value |
|---|---|---|---|
| *n* | 149 (15%) | 125 (12%) | |
| Sex | | | |
| Male | 21% | 43% | <0.001 |
| Female | 79% | 57% | <0.001 |
| Ratio (M/F) | 1:3.8 | 1:1.3 | |
| Mean age, diagnosis (years ± SD) | 25.4 ± 3.6 | 71.7 ± 4.4 | |
| Range | 18–30 | 65–83 | |
| Symptom duration (mean, years ± SD) | 5.8 ± 12.0 | 6.14 ± 12.6 | 0.119 |

**Table 2** Modes of presentation of illness

| Presentation | Age 18–30 years | Age ≥65 years | *p*-value |
|---|---|---|---|
| *n* | 149 | 125 | |
| Diarrhea[a] | 49% | 50% | 0.921 |
| Anemia | 7% | 11% | 0.275 |
| Bone disease | 3% | 7% | 0.151 |
| Screening | 13% | 7% | 0.096 |
| Incidental | 3% | 9% | 0.056 |
| Other[b] | 24% | 16% | 0.096 |

[a] Diarrhea in elderly males versus young adult males, $p = 0.006$

[b] Other presentations include dermatitis herpetiformis, abdominal pain, fatigue, neuropathy, and weight loss

**Table 3** Histological findings

| Pathology | Age 18–30 years $n = 114$ (%) | Age ≥65 years $n = 100$ (%) | *p*-value |
|---|---|---|---|
| ↑IEL | 4 (4) | 1 (1) | 0.248 |
| PVA | 51 (45) | 43 (43) | 0.977 |
| STVA | 16 (14) | 12 (12) | 0.758 |
| TVA | 42 (37) | 44 (44) | 0.231 |

↑*IEL* intraepithelial lymphocytosis (Marsh I and II)

*PVA* partial villous atrophy: Marsh IIIa

*STVA* subtotal villous atrophy: Marsh IIIb

*TVA* total villous atrophy: Marsh IIIc

elderly cohort and 49% in the young adult group ($p = 0.921$). The majority of patients who presented with diarrhea in each age group were female, 85% and 63% in the young adult and elderly cohorts, respectively. A greater percentage of men in the elderly group presented with diarrhea compared to the young male adults, 37% versus 15%, respectively ($p = 0.006$). There were otherwise no gender differences in the mode of presentation of celiac disease.

## Diagnosis

Serologic data were available for 87% of the patients in the young adult group and 85% of the patients in the elderly cohort. The specific serologic assay used in this study was the tissue transglutaminase (tTG) IgA antibody assay. Seventy percent of the younger cohort had positive tTG-IgA antibodies compared to 60% of the elderly group. Review of the biopsies revealed no statistically significant difference in the degree of villous atrophy between each group (Table 3).

## Associated Diseases

The prevalence of diseases associated with celiac disease is shown in Table 4. Autoimmune disease was similarly prevalent in the elderly and young adult groups, 26% versus 19% ($p = 0.133$). A further break-down of the frequency of autoimmune disease by specific illness is shown in Table 5. Thirty-three patients in the elderly cohort had one or more autoimmune condition compared to 28 patients in the young adult group. Among the listed conditions, Raynaud's disease occurred more often in the young adults while polymyalgia rheumatica, rheumatoid arthritis, Sjögren's disease, and pernicious anemia were more common among the elderly. We found that thyroid disease occurred with greater frequency in the elderly age group compared to the young adults, at 14% versus 7% ($p = 0.037$). Neuropathy was also more common in the elderly compared to young adults, at 11% versus 4% ($p = 0.023$). The proportion of patients with dermatitis

**Table 4** Associated diseases

| Associated diseases | Age 18–30 years No. (%) | Age ≥65 years No. (%) | *p*-value |
|---|---|---|---|
| Autoimmune disease (total) | 28 (19) | 33 (26) | 0.133 |
| Neuropathy | 6 (4) | 12 (11) | 0.023 |
| Thyroid disease | 10 (7) | 18 (14) | 0.037 |
| Dermatitis herpetiformis | 10 (7) | 10 (8) | 0.392 |

**Table 5** Frequency of autoimmune disease

| Autoimmune diseases[a] | Age 18–30 years (No.) | Age ≥ 65 years (No.) |
|---|---|---|
| Insulin-dependent diabetes mellitus | 2 | 1 |
| Raynaud's disease | 3 | 1 |
| Systemic lupus erythematosus | 2 | 1 |
| Multiple sclerosis | 1 | 0 |
| Myasthenia gravis | 1 | 0 |
| Vitiligo | 1 | 1 |
| Hashimoto's disease | 1 | 2 |
| Graves' disease | 1 | 0 |
| Alopecia | 1 | 0 |
| Psoriasis | 3 | 2 |
| Autoimmune neutropenia | 1 | 0 |
| Inflammatory bowel disease | 3 | 4 |
| Polymyositis | 0 | 1 |
| Polymyalgia rheumatica | 0 | 3 |
| Rheumatoid arthritis | 0 | 2 |
| Sjögren's syndrome | 0 | 3 |
| Pernicious anemia | 0 | 2 |
| Hypothyroidism | 8 | 16 |

[a] Some patients had more than one autoimmune disease

herpetiformis was similar in each group, 7% and 8%, for the young adults and elderly, respectively,

### Bone Disease

The frequency of bone disease in our study population is shown in Table 6. We only included patients who underwent DEXA scans within 1 year of diagnosis of celiac disease. Among the 46 patients in the young adult group and 38 patients in the elderly cohort, 29% of the young adults and 61% of the elderly patients had BMD findings consistent with osteopenia or osteoporosis. When we compared the bone density results to sex-specific population-values, we found that in the young adult group, males had *T*-scores at the hip that were 0.64 ± 1.52 SD below the peak BMD for this population ($p = 0.11$). Similarly, *Z*-scores were 0.22 ± 1.02 SD ($p = 0.55$) below the peak BMD in sex- and age-matched controls; neither finding was statistically significant. When we compared the BMD in young adult females with celiac disease to sex-specific population values, we found that *T*-scores at the hip were 0.74 ± 1.28 SD units below the norm ($p = <0.001$) and *Z*-scores were 0.41 ± 1.00 SD units below peak BMD for this population ($p = 0.06$; Tables 7, 8).

When the BMD scores for elderly patients with celiac disease were compared to population-expected values, elderly males had a mean hip *T*-score of 1.50 ± 1.83 SD units below the expected sex-specific peak BMD ($p = <0.001$). However, their sex- and age-specific *Z*-score of −0.20 ± 1.32 did not differ significantly from the reference group ($p = 0.50$). In elderly female patients with celiac disease, the mean hip *T*-score was 2.16 ± 1.03 SD units below the sex-matched peak BMD ($p = <0.001$), although the age- and sex-specific mean total hip *Z*-score of 0.08 ± 1.58 did not differ significantly from a healthy reference group ($p = 0.80$). When *Z*-scores at the hip were compared between elderly and young adults with celiac disease, there was no statistically significant difference by age or gender (Table 8).

**Table 6** Bone disease

| | Age 18–30 years (%) | Age ≥65 years (%) |
|---|---|---|
| *n* (%)[a] | 46 (32) | 38 (30) |
| Osteoporosis (Hip) | 7 | 28 |
| Osteopenia (Hip) | 22 | 33 |
| Normal DEXA scan | 71 | 39 |

[a] *n* total number of patients with a DEXA scan within 1 year of diagnosis

## Discussion

Few studies have rigorously analyzed the clinical characteristics of celiac disease in the elderly, and no prior study has compared the presentation of celiac disease in the elderly with young adults. Studies reveal that celiac disease occurs in about 1% of both adults and children [14, 15]. Based on this prevalence data, we can assume that the majority of adults most likely had disease in childhood. One would expect elderly patients to have more severe disease given their longer duration of illness. However, the development of new disease in the elderly who were previously without celiac disease [16] argues for the development of de novo celiac disease in the elderly. In the screening study performed in Finland by Vilppula et al. [16] biopsy-proven celiac disease was present in 2.34% of 2,216 individuals >55 years of age. Five of the newly diagnosed patients in their study were previously negative on testing.

Overall, we found no significant difference in the presentation of celiac disease in elderly patients compared to young adults. There was a similar duration of symptoms, which was a surprising result. We had expected a longer duration of symptoms in older patients. The factors accounting for a delay in diagnosis are likely multi-factorial: physicians may lack awareness of celiac disease and not test for it and patients may present with atypical symptoms or asymptomatic disease. Another factor that can potentially delay diagnosis is if a patient has previously been tested for celiac disease and found to be negative. A

**Table 7** Deviation of observed *T*-scores and *Z*-scores in patients with celiac disease compared to population-expected values, by age group

| Gender | Group | *N* | 18–30 years | | *N* | ≥65 years | |
|---|---|---|---|---|---|---|---|
| | | | *T*-score Mean ± SD | *Z*-score Mean ± SD | | *T*-score Mean ± SD | *Z*-score Mean ± SD |
| Male | Population expected | | 0.00 ± 1.00 | 0.00 ± 1.00 | | 0.00 ± 1.00 | 0.00 ± 1.00 |
| | Celiac observed | 9 | −0.64 ± 1.52 | −0.22 ± 1.02 | 18 | −1.50 ± 1.83 | −0.20 ± 1.32 |
| Female | Population expected | | 0.00 ± 1.00 | 0.00 ± 1.00 | | 0.00 ± 1.00 | 0.00 ± 1.00 |
| | Celiac observed | 37 | −0.74 ± 1.28 | −0.41 ± 1.00 | 20 | −2.16 ± 1.03 | 0.08 ± 1.58 |
| All patients | Population expected | | 0.00 ± 1.00 | 0.00 ± 1.00 | | N/A | N/A |
| | Celiac observed | 46 | −0.72 ± 1.31 | −0.37 ± 0.99 | 38 | −1.85 ± 1.48 | −0.05 ± 1.45 |

**Table 8** Bone disease comparisons, by age group

| | *p*-value |
|---|---|
| Young adults with celiac disease | |
| Young male celiac vs. population expected (*T*-score) | 0.11 |
| Young male celiac vs. population expected (*Z*-score) | 0.55 |
| Young female celiac vs. population expected (*T*-score) | <0.001 |
| Young female celiac vs. population expected (*Z*-score) | 0.06 |
| Elderly with celiac disease | |
| Elderly male celiac vs. population expected (*T*-score) | <0.001 |
| Elderly male celiac vs. population expected (*Z*-score) | 0.5 |
| Elderly female celiac vs. population expected (*T*-score) | <0.001 |
| Elderly female celiac vs. population expected (*Z*-score) | 0.8 |
| Elderly vs. young adults with celiac disease | |
| Elderly male celiac vs. young male celiac (*Z*-score) | 0.97 |
| Elderly female celiac vs. young female celiac (*Z*-score) | 0.16 |

study by Collin et al. [17] illustrated this point. They found that 28% of patients with potential celiac disease eventually developed various degrees of villous atrophy on follow-up endoscopy performed between 1 and 7 years after the initial negative endoscopy. Similarly, Vilppula et al. [16] found five new cases among patients who had previously been seronegative; two had minor abdominal symptoms and three were asymptomatic. Thus, a negative biopsy does not preclude the subsequent development of celiac disease.

Our data did not show that disease severity is increased in elderly patients compared to young adults. In fact, the modes of presentation of illness were remarkably similar between the two groups. Diarrhea was the major presenting symptom in both groups. This was an unexpected finding in the elderly celiac patients since they have been reported to typically present with milder gastrointestinal complaints such as bloating and even constipation as opposed to classic symptoms of malabsorption [18].

In terms of gender differences, our study showed a female predominance for celiac disease, as reported in the literature [19], but this was more marked in the young adult group, 3.8:1 compared to 1.3:1 in the elderly cohort. This contrasts with findings in the literature that female predominance tends to be greater in elderly patients compared to young adults [20, 21]. One of the factors that could account for this finding was a greater number of females in the young adult group compared to the elderly cohort at baseline, 79% versus 57%. While females are more frequently diagnosed with celiac disease, serological screening studies reveal a similar male to female prevalence [22].

Autoimmune illness was similarly prevalent in the two age groups. Up to 26% of patients had an autoimmune illness that is markedly higher than the 3% prevalence for autoimmune disease in the general population [23]. One significant difference was that neuropathy and thyroid disease were more common in the elderly cohort. It has been extensively reported in the literature that thyroid disease, specifically hypothyroidism, is increased in adult patients with celiac disease compared to the general population [24–29]. In our study, 14% of the elderly had thyroid disease. This correlates with prevalence data for thyroid disease from other studies, which are similarly increased. For example, a Brazilian study of adult patients with celiac disease found that 19.2% of the patients had thyroid disease [30]. In contrast, the prevalence of thyroid disease in non-celiac elderly in the general population is around 10% [24–29], which is only slightly lower than the prevalence of 14% observed in the elderly celiacs in our study. Even in our young adult population, the prevalence of thyroid disease was 7%, which is higher than the 3–5% prevalence seen in the non-celiac adult population [24–29]. These findings suggest that the increased prevalence of thyroid disease in celiac patients, both young and old, is a function of the underlying disease process as opposed to age effect alone, particularly in the elderly. It is striking that there was a similar rate of autoimmune diseases in the young adult and elderly cohort since it is often considered that the elderly have an increased rate of autoimmune diseases.

Similar to autoimmune disease, we found that dermatitis herpetiformis was equally prevalent in the two groups. However, based on the literature, its prevalence tends to be increased in elderly men [31, 32]. We did not observe such

a finding. Instead, more women than men in both age groups had dermatitis herpetiformis.

There was no difference in the degree of villous atrophy in the young adult and elderly cohorts, which suggests that the elderly patients in our study may have had milder, long-standing disease or, possibly, de novo illness. The number of patients with increased intraepithelial lymphocytosis, the mildest pathological lesion, was quite small. Interestingly, four out of these five patients presented with diarrhea. This finding underscores the fact that clinical symptoms in celiac disease often do not correlate with the degree of villous atrophy [33, 34].

In general, we were confident in our diagnosis of celiac disease because all were biopsy-proven and we had serologic data to confirm our biopsy results. Serologic data were available for 85% and 87%, respectively, of our elderly and young adult patients, and there was minimal difference in the degree of positive tTG-IgA by age group. This helps to support the fact that seroprevalence is not diminished in elderly patients. In fact, there is no data to suggest that the serologic response in elderly patients is different from that of young adults [8].

Numerous studies have shown that bone disease, specifically osteoporosis, is more common in patients with celiac disease compared to the general population. As such, screening for osteoporosis and osteopenia is recommended in this patient population [35–37]. Various etiologies have been raised to explain this observation including deficiencies in calcium and vitamin D secondary to malabsorption as well as the presence of circulating anti-bone auto-antibodies [38]. We analyzed the mean BMD of patients with celiac disease using DEXA scan measurements. As expected, bone disease was more common in elderly celiac patients compared to younger celiac patients. However, when we compared elderly celiac patients with elderly non-celiac patients for the presence of bone disease, there was no significant difference in terms of their *Z*-score. This was a surprising finding since one would expect celiac disease to confer an independent and/or additive risk for bone disease separate from age-effect alone. The only statistically significant difference was a lower-than-expected *T*-score for elderly men with celiac disease. Interestingly, female patients with celiac disease in both age groups had lower-than-expected *T*-scores that were statistically significant, although their *Z*-scores were not significantly different. Another unexpected finding was that the *Z*-score was similar for both elderly and young celiac patients; one would expect a greater degree of bone loss in the elderly celiac cohort. While the reasons for this finding are not clear, one possible explanation is that bone disease in celiac patients may be related to an early onset of impaired bone formation due to malabsorption, secondary to anti-bone auto-antibodies, or a combination of these factors. This pathway could lead to an accelerated and early rate of reduced peak bone mass as seen in younger celiac patients. In contrast, in elderly celiac patients, bone remodeling activity may be less affected by the underlying pathogenesis of celiac disease and more subject to age-effect. However, there is scant literature on this topic.

Our study has a few limitations that are worth noting. Since we studied a highly selected population in a single tertiary center, we were limited in our ability to generalize our results to larger population samples. However, the sample size of elderly patients in this study is the largest reported in the literature. Another limitation in our bone-disease analysis is that not every patient was scanned using the same bone densitometry scanner from which the population reference values were derived.

Despite these limitations, our study provides important and novel data on an under-reported population of patients with celiac disease and highlights the fact that there is still much to be learned about this disease process. Given that the prevalence of celiac disease continues to rise in the elderly age group, it is imperative that physicians have a high index of suspicion for this illness to prevent further morbidity and mortality in their older patients. Indeed, larger multi-center studies are required to further discern the effect of age on disease presentation and the factors that trigger disease at any given age. Our data of similar clinical and histological manifestations of celiac disease in the elderly as well as young adults argue for the de novo development of celiac disease in the elderly.

## References


1. Green PH, Cellier C. Celiac disease. *N Engl J Med*. 2007;357:1731–1743.
2. Fasano A, Berti I, Gerarduzzi T, et al. Prevalence of celiac disease in at-risk and not-at-risk groups in the United States: a large multicenter study. *Arch Intern Med*. 2003;163(3):286–292.
3. Cook HB, Burt MJ, Collett JA, et al. Adult coeliac disease: prevalence and clinical significance. *J Gastroenterol Hepatol*. 2000;15(9):1032–1036.
4. Baroni F, Ghisla MK, Leonardi R, Grassi V. Celiac disease in the elderly: a case report. *Ann Ital Med Int*. 2005;20(4):253–257.
5. Freeman HJ. Adult celiac disease in the elderly. *World J Gastroenterol*. 2008;14(45):6911–6914.
6. Talal AH, Murray JA, Goeken JA, et al. Celiac disease in an adult population with insulin-dependent diabetes mellitus: use of endomysial antibody testing. *Am J Gastroenterol*. 1997;92(8):1280–1284.
7. Counsell CE, Ruddell WS. Association between coeliac disease and autoimmune thyroid disease. *Gut*. 1995;36(3):475–476.
8. Rashtak S, Murray JA. Celiac disease in the elderly. *Gastroenterol Clin N Am*. 2009;38:433–446.
9. Hankey GL, Holmes GK. Coeliac disease in the elderly. *Gut*. 1994;35(1):65–67.
10. Johnson MW, Ellis HJ, Asante MA, Ciclitira PJ. Celiac disease in the elderly. *Nat Clin Pract Gastroenterol Hepatol*. 2008;5:697–706.

11. Lohi S, Mustalahti K, Kaukinen K, et al. Increasing prevalence of coeliac disease over time. *Aliment Pharmacol Ther*. 2007;26(9): 1217–1225.
12. Marsh MN. Gluten, major histocompatibility complex, and the small intestine. A molecular and immunobiologic approach to the spectrum of gluten sensitivity ('celiac sprue'). *Gastroenterology*. 1992;102:330–354.
13. Oberhuber G, Granditsch G, Vogelsang H. The histopathology of coeliac disease: time for a standardized report scheme for pathologists. *Eur J Gastroenterol Hepatol*. 1999;11:1185–1194.
14. West J, Logan RF, Hill PG, et al. Seroprevalence, correlates, and characteristics of undetected coeliac disease in England. *Gut*. 2003;52:960–965.
15. Bingley PJ, Williams AJ, Norcross AJ, Unsworth DJ, Lock RJ, Ness AR, Jones RW. Undiagnosed coeliac disease at age seven: population-based prospective birth cohort study. *BMJ*. 2004; 7:328(7435):322–323.
16. Vilppula A, Kaukinen K, Luostarinen L, et al. Increasing prevalence and high incidence of celiac disease in elderly people: a population-based study. *BMC Gastroenterol*. 2009;9:49.
17. Collin P, Helin H, Maki M, Hallstrom O, Karvonen AL. Follow-up of patients positive in reticulin and gliadin antibody tests with normal small-bowel biopsy findings. *Scand J Gastroenterol*. 1993;28(7):595–598.
18. Marmouz F. Adult coeliac disease. *Eur Ann Allergy Clin Immunol*. 2007;39:23–25.
19. Ivarsson A, Persson LA, Nystrom L, Hernell O. The Swedish coeliac disease epidemic with a prevailing twofold higher risk in girls compared to boys may reflect gender specific risk factors. *Eur J Epidemiol*. 2003;18:677–684.
20. Murray JA, Van Dyke C, Plevak MF, et al. Trends in the identification and clinical features of celiac disease in a North American community, 1950–2001. *Clin Gastroenterol Hepatol*. 2003;1(1):19–27.
21. Swinson CM, Levi AJ. Is coeliac disease underdiagnosed? *Br Med J*. 1980;281(6250):1258–1260.
22. Rubio-Tapia A, Kyle RA, Kaplan EL, Murray JA, et al. Increased prevalence and mortality in undiagnosed celiac disease. *Gastroenterology*. 2009;137(1):88–93.
23. Jacobson DL, Gange SJ, Rose NR, Graham NM. Epidemiology and estimated population burden of selected autoimmune diseases in the United States. *Clin Immunol Immunopathol*. 1997;84: 223–243.
24. Elfstrom P, Montgomery SM, Kampe O, et al. Risk of thyroid disease in individuals with celiac disease. *J Clin Endocrinol Metabol*. 2008;93(10):3915–3921.
25. Vanderpump MPJ, Tunbridge WMG, French JM, et al. The incidence of thyroid disorders in the community: a 20-year follow-up of the Whickham survey. *Clin Endocrinol*. 2005;43(1): 55–68.
26. Sundbeck G, Lundberg PA, Lindstedt G, Jagenburg R, Eden S. Incidence and prevalence of thyroid disease in elderly women: results from the longitudinal population study of elderly people in Gothenburg, Sweden. *Age Ageing*. 1991;20:291–298.
27. Bemben DA, Winn P, Hamm RM, Morgan L, Davis A, Barton E. Thyroid disease in the elderly. Part 1. Prevalence of undiagnosed hypothyroidism. *J Fam Pract*. 1994;38:577–582.
28. Bemben DA, Hamm RM, Morgan L, Winn P, Davis A, Barton E. Thyroid disease in the elderly. Part 2. Predictability of subclinical hypothyroidism. *J Fam Pract*. 1994;38:583–588.
29. Muller GM, Levitt NS, Louw SJ. Thyroid dysfunction in the elderly. *S Afr Med J*. 1997;87:1119–1123.
30. da Silva Kotze LM, Nisihara RM, da Rosa Utiyama SR, Piovezan GC, Kotze LR. Thyroid disorders in Brazilian patients with celiac disease. *J Clin Gastroenterol*. 2006;40:33–36.
31. Gawkrodger DJ, Blackwell JN, Gilmour HM, et al. Dermatitis herpetiformis: diagnosis, diet and demography. *Gut*. 1984;25(2): 151–157.
32. Oxentenko AS, Murray JA. Celiac disease and dermatitis herpetiformis: the spectrum of gluten-sensitive enteropathy. *Int J Dermatol*. 2003;42:585–587.
33. Brar P, Kwon GY, Egbuna I, et al. Lack of correlation of degree of villous atrophy with severity of clinical presentation of coeliac disease. *Dig Liver Dis*. 2007;39:26–29.
34. Murray JA, Rubio-Tapia A, Van Dyke CT, et al. Mucosal atrophy in celiac disease: extent of involvement, correlation with clinical presentation, and response to treatment. *Clin Gastroenterol Hepatol*. 2008;6:186–193.
35. Armagan O, Uz T, Tascioglu F, Colak O, Oner C, Akgun Y. Serological screening for celiac disease in premenopausal women with idiopathic osteoporosis. *Clin Rheumatol*. 2005;24:239–243.
36. Stenson WF, Newberry R, Lorenz R, Baldus C, Civitelli R. Increased prevalence of celiac disease and need for routine screening among patients with osteoporosis. *Arch Intern Med*. 2005;165:393–399.
37. Meyer D, Stavropolous S, Diamond B, Shane E, Green PH. Osteoporosis in a North American adult population with celiac disease. *Am J Gastroenterol*. 2001;96:112–119.
38. Shaoul R, Lerner A. Associated autoantibodies in celiac disease. *Autoimmune Rev*. 2007;6(8):559–565.