

The prevalence of celiac disease in patients with fibromyalgia

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The prevalence of celiac disease in the general population is around 1%. However, based on our current study, the prevalence of celiac disease in the fibromyalgia population is 3%. Individuals with celiac disease frequently present with symptoms similar to fibromyalgia, suggesting a link between the two.

This study aims to better delineate the concomitant prevalence rate of celiac disease in our fibromyalgia cohort and to determine if concomitant screening should be undertaken.

Given the overlapping clinical features, differing treatment paradigms, and the previously reported potential improvement of symptoms with a gluten-free diet, patients with fibromyalgia should also be screened for celiac disease.

This study was a retrospective chart review. The prevalence of celiac disease was computed. A two-sided chi-square test was used to determine significance. All patients evaluated from November 22, 2014, through December 31, 2015, at our tertiary referral fibromyalgia clinic were considered for the study. Patients with a validated diagnosis of fibromyalgia were then assessed for celiac disease.

Of 1,133 charts reviewed, 955 met the diagnostic criteria for fibromyalgia; 542 of these patients had information regarding celiac disease. Of these, 16 patients were found to have celiac disease. Therefore, the prevalence of celiac disease in our fibromyalgia cohort was 3% (16/542) ($p < 0.001$).

In patients presenting with fibromyalgia, screening for celiac disease should be performed due to the three-fold increase in the comorbid prevalence rate of celiac disease in our fibromyalgia cohort than that reported for the general population.

Fibromyalgia is a common centralized pain-sensitivity syndrome characterized by chronic widespread musculoskeletal pain, fatigue, and sleep disturbance that affects up to 8% of the population.¹ Studies have shown that gastrointestinal (GI) symptoms are common in this population, with as many as 73% of individuals reporting GI symptoms, with food sensitivities increasing.^{2,3} In one study, 30% of fibromyalgia patients reported the need to modify their diets, while 7% reported having been diagnosed with a food allergy or intolerance.⁴ Fibromyalgia is associated with substantial morbidity and cost. The annual, mean health care costs are three to four times higher in individuals with fibromyalgia.^{5,6} Indirect societal costs from lost wages and disability have been estimated to be a staggering 12 times higher in patients with fibromyalgia.⁵

Celiac disease is an autoimmune disease characterized by small bowel inflammation that leads to the loss of normal villous architecture due to antibody formation in response to gluten ingestion. The prevalence of celiac disease in the general population is around 1%.^{7,8} Celiac disease has gained increased attention in recent years

because individuals frequently present with extra-intestinal symptoms, such as myalgia, arthralgia, fatigue, and psychological symptoms, which are similar to fibromyalgia symptoms.⁹ These shared symptoms suggest a possible link—specifically gluten—

between fibromyalgia and celiac disease. Several studies^{2,3,9,10} support this potential link. In a nationwide survey of individuals with celiac disease, 9% reported being diagnosed with fibromyalgia before being diagnosed with celiac disease.⁹ In a study of 90 patients with fibromyalgia, one patient had celiac disease, which is a slightly higher prevalence than in the general population.¹⁰ Moreover, studies^{11,12} observed substantial clinical improvements in fibromyalgia symptoms when patients adhered to a gluten-free diet, which further suggests a link between fibromyalgia and gluten. Despite this potential link, the treatments for these two conditions differ significantly. The multimodal treatment approach of fibromyalgia primarily focuses on symptom management with medications and non-medication treatment strategies. In contrast, celiac disease can be effectively treated with a strict gluten-free diet.

Given the possible overlap between fibromyalgia and celiac disease and the inherent differences in treatment approaches, determining the correct diagnosis and possibly a concomitant diagnosis are imperative for patient care. In order to determine the need for concomitant screening, the

TABLE 1

Demographic characteristics of fibromyalgia patients (n = 955)

CHARACTERISTICS	VALUES
Sex (female), %	83.3
Tobacco use, %	14.8
Benzodiazepine use, %	29.9
Opioid use, %	31.4
Employed, %	49.9
Widespread Pain Index score, mean (SD)	11.90 (4.09)
Symptom Severity Scale score, mean (SD)	8.48 (2.10)
Tender point count, mean (SD)	14.06 (4.52)
PHQ-9 ^a depression score, mean (SD)	11.71 (5.87)
GAD-7 ^b anxiety score, mean (SD)	8.35 (6.00)

^aPHQ-9, Patient Health Questionnaire-9; ^bGeneralized Anxiety Disorder-7.

prevalence of celiac disease in patients with fibromyalgia needs to be more clearly defined.¹³ In this study, the goal was to better delineate the prevalence rate of celiac disease in patients with fibromyalgia in our tertiary academic referral center.

Methods

Retrospective description and patient selection

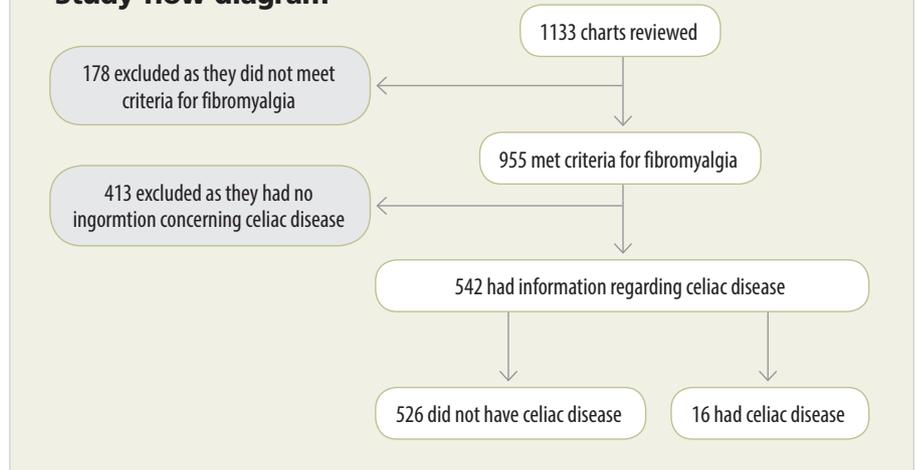
This study was designed as a retrospective chart review. The Mayo Clinic Institutional Review Board approved the study and waived the requirement for informed consent. A database was compiled from electronic health records (EHRs) of all patients who were evaluated at the Mayo Clinic Fibromyalgia and Chronic Fatigue Clinic (FCFC) from November 22, 2014, through December 31, 2015. An in-depth medical record review was performed. The patients' EHRs were first assessed for the presence of a validated diagnosis of fibromyalgia, which had to be given by a physician or nurse practitioner in the FCFC via the 1990 and/or 2010 American College of Rheumatology Fibromyalgia Classification Criteria.^{14,15} Patients not meeting the formal diagnostic criteria for fibromyalgia were excluded from the study.

Patients who met the diagnostic criteria for fibromyalgia then had to have been assessed for the presence of celiac disease by a small bowel biopsy, our institution's celiac disease serology cascade, or the presence of the diagnosis provided by an outside institution. Patients were considered to have celiac disease if they had pathologic findings of small bowel biopsy that were consistent with celiac disease, if our institution's celiac disease serology cascade was positive, or if the diagnosis from an outside institution had corresponding clinical features. If there was no information concerning celiac disease in the EHR, the patient was excluded. Our institution's celiac disease serology cascade algorithm is shown in Figure 2.

Patient records were also assessed for age, sex, smoking status, employment status, current opioid use, current benzodiazepine use, fibromyalgia-specific clinical scores (Symptom Severity Score,

FIGURE 1

Study flow diagram



Widespread Pain Index, and tender point count), Patient Health Questionnaire (PHQ)-9 depression score, Generalized Anxiety Disorder (GAD)-7 score, presence of GI symptoms, and various laboratory studies including, hemoglobin, erythrocyte sedimentation rate, 25-hydroxy vitamin D, thyroid stimulating hormone, cortisol, C-reactive protein, and antinuclear antibody.

Statistical analysis

The prevalence of celiac disease was computed using a ratio of the total number of fibromyalgia patients with confirmed celiac disease as the numerator and the total number of fibromyalgia patients who had been assessed for celiac disease as the denominator. A two-sided chi-square test was used to determine statistical significance.

TABLE 2

Gastrointestinal symptoms in patients with fibromyalgia

SYMPTOM	PERCENTAGE (N = 955)
Any symptom below	91.0
Pain or cramps in the lower abdomen	53.2
Heartburn	41.8
Nausea	52.7
Loss of appetite	35.9
Bowel cramps	43.4
Frequent loose stools	41.3
Constipation	51.1
Food sensitivities	52.6

Results

We reviewed EHRs for 1,133 patients (Fig. 1). Detailed results regarding demographics, fibromyalgia-specific clinical scores, depression and anxiety scores, presence of various GI symptoms, and the results of numerous laboratory studies are shown in Tables 1 to 3. Of these 1,133 patients, 955 met the diagnostic criteria for fibromyalgia. Of these, 542 had been assessed (had information available) for celiac disease from pathologic findings of a small bowel biopsy, results from our institutional celiac disease serology cascade, or an outside institution with corresponding clinical features. Of these, 16 patients were found to have celiac disease. Therefore, the calculated concomitant prevalence (16/542) of celiac disease in our fibromyalgia cohort was 3% (p < 0.001).

Discussion

The prevalence of celiac disease in our fibromyalgia cohort was 3%, which represents a three-fold increase in the prevalence of celiac disease compared to that seen in the general population.^{7,8} To our knowledge, this is the first study to show an increased prevalence of celiac disease in individuals with concomitant fibromyalgia.

GI symptoms were very common in our study. In total, 91% of our patients reported GI symptoms; this is a substantially higher percentage than that reported in a previous study aimed at describing the prevalence of GI symptoms, specifically in relation to irritable bowel syndrome in patients with fibromyalgia.² In contrast, we assessed several additional GI symptoms, including food sensitivities, constipation, frequent loose stools, bowel cramps, loss

of appetite, nausea, and heartburn. In our cohort, 52.7% reported nausea, 41.3% reported frequent loose stools, and 51.1% reported constipation, which exceeded the respective 21%, 9%, and 12% reported by Triadafilopoulos et al.² Given these differences, GI symptoms are likely more common in the fibromyalgia population than previously documented in the medical literature.

Currently, the World Gastroenterology Organization Global Guidelines on Celiac Disease¹⁶ recommend considering the possibility of celiac disease in individuals with a variety of symptoms, even if they appear to be asymptomatic from a GI perspective. Given the increased prevalence of celiac disease in patients with fibromyalgia, as observed in the current study, it is suggested that screening for celiac disease, specifically serological tests¹⁷, should be done in this patient population.

Although fibromyalgia and celiac disease may coexist, the treatment of these two conditions differs greatly. Despite the differing treatment modalities, which Rodrigo et al.¹¹ noted, substantial extra-

TABLE 3

Laboratory results in fibromyalgia-specific patients

LABORATORY TEST	RESULT, MEAN (SD)
Hemoglobin	13.49 (1.28)
Erythrocyte sedimentation rate	10.62 (9.77)
25-hydroxy vitamin D	37.0 (15.9)
Thyroid stimulating hormone	2.53 (3.26)
Cortisol	10.47 (4.84)
C-reactive protein	5.44 (6.02)
Antinuclear antibody	0.62 (1.18)

intestinal improvements were seen when seven patients with fibromyalgia adhered to a gluten-free diet. These results suggested that if the autoimmune inflammatory process is better controlled, then the underlying central sensitization associated with fibromyalgia may also improve. In addition, patients with non-celiac gluten sensitivity have similar symptoms to those with celiac disease. In contrast to celiac disease, non-celiac gluten sensitivity is thought to be mediated by the innate im-

mune system; thus, serologic markers are normal. The prevalence of non-celiac gluten sensitivity is largely unknown, but it has been noted that 1.1% of patients without celiac disease consume a gluten-free diet.¹⁸ In comparison, in another study, the frequency of non-celiac gluten sensitivity was shown to be about 30% in patients with irritable bowel syndrome.¹⁹ If the prevalence of non-celiac gluten sensitivity similarly increases in the fibromyalgia population, it may be that a considerable portion of fibromyalgia patients could potentially benefit from a gluten-free diet.

Limitations of our study include the use of serologic tests primarily to diagnose celiac disease in our cohort. According to a systematic review, the sensitivity of tTg antibodies is 93% with specificity over 99%.¹⁷ However, the reference criterion remains an upper endoscopy with biopsy of the duodenum, interpreted by a trained pathologist. Therefore, the use of serologic tests may have underestimated or overestimated the true prevalence of celiac disease in our fibromyalgia cohort. Furthermore, our patient population is unique because all were seen in a specialized fibromyalgia clinic at a tertiary care center, which likely resulted in a group of individuals with more severe fibromyalgia symptoms (Table 1). Whether the severity of symptoms in this cohort influenced the prevalence of celiac disease compared with that in the overall fibromyalgia population is unclear.

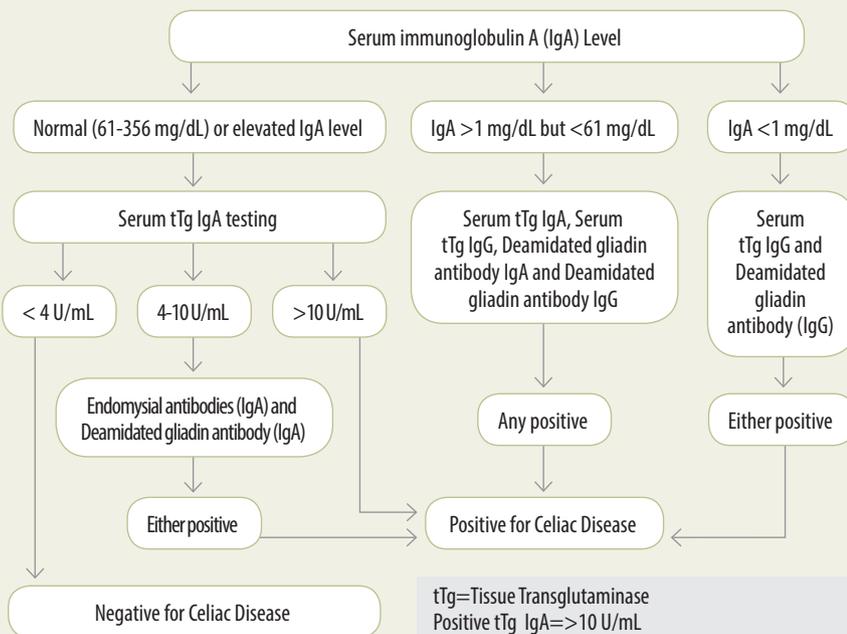
This study was retrospective and was not designed to prospectively study the relationship between fibromyalgia symptoms and celiac disease or gluten ingestion. It is unknown if patients with a dual diagnosis of fibromyalgia and celiac disease have more severe symptoms than fibromyalgia patients without celiac disease. Also unknown is the extent of improvement fibromyalgia patients with celiac disease experience with a gluten-free diet. These are all topics that warrant additional investigation.

Recommendation

The concomitant prevalence of celiac disease in our fibromyalgia cohort was 3%, representing a three-fold higher rate

FIGURE 2

Celiac disease serology cascade



tTg=Tissue Transglutaminase
 Positive tTg IgA=>10 U/mL
 Positive tTg IgG=>6 U/mL
 Positive deamidated gliadin antibody IgA=>20 U
 Positive deamidated gliadin antibody IgG=>20 U
 Positive endomysial antibodies=positive result
 Positive ***

than that of the general population. Given the overlapping clinical features, differing treatment paradigms, and the previously reported potential improvement of symptoms with a gluten-free diet, patients with fibromyalgia should also be screened for celiac disease. **MM**

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