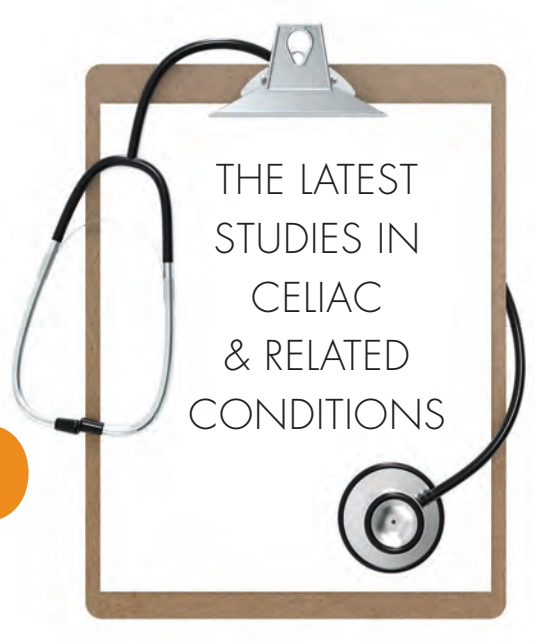
Research Roundup



Is there a gender difference in clinical symptoms between men and women affected by celiac disease?

In our clinic, we see definitive gender differences between men and women affected by celiac disease and gluten intolerance. A recent study has addressed this issue in detail.

Clinical presentations of celiac have demonstrated differences between symptoms among women and men. This study evaluated the differences in the clinical presentation of celiac among Brazilian men and women at the time of diagnosis.

The study focused on symptoms and clinical signs of 240 patients (80 [33.3 percent] men and 160 [66.6 percent] women) aged >18 years who were diagnosed with celiac during 2000-2017. The overall mean age at diagnosis was 38.3 ± 13.28 years, with the mean age being 38.1 ± 14.48 years for men and 38.4 ± 12.68 years for women ($p = 0.16$). Details regarding other previously diagnosed autoimmune diseases were requested of the patient.

Symptoms such as anxiety/depression, lack of appetite, flatulence, malaise, nausea, and vomiting were more frequent in females than males. Only steatorrhea (increased fat concentration in the stool) was more frequent in men. Clinical signs such as anemia, short stature, and weight loss were also more frequent in women. Other findings such as diarrhea, abdominal distension or pain, and anorexia did not reveal differences in terms of gender. Regarding associated autoimmune diseases, dermatitis herpetiformis was more frequent in men, and thyroiditis was more frequent in women.

The study demonstrated that men and women with celiac presented differences in clinical presentation at the time of diagnosis. Women exhibited more gastrointestinal symptoms and clinical signs than men.

> **Gender-related differences in celiac patients at diagnosis.** *Archives of Medical Research.* 2019 Nov 27; 50(7):437-441. Lima, RF., Maria da Silva Kotze, L., et al.

Can celiac disease affect female fertility?

An increased risk of reproductive failures in women with celiac disease has been shown by several studies. A new study analyzes the prevalence and seroprevalence of celiac in women with recurrent reproductive failure.

A retrospective study was performed in a single infertility clinic from September 2016 to December 2017. A total of 690 women with unexplained history of recurrent miscarriage and/or recurrent implantation failure were consecutively recruited. IgA anti-transglutaminase 2 (TG2) antibody data was collected, as well as IgG anti-TG2 and IgA/IgG anti-deamidated gluten peptide (DGP) data in

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most cases, and IgG anti-gliadin antibodies occasionally. In selected women, HLA-DQ genotyping was requested. Biopsy was suggested to all women with positive serological results or belonging to celiac risk groups. Reproductive outcomes were recorded from women with high suspicion of celiac and a control group comprised of 49 women.

Anti-TG2-positive women comprised 1 percent of the sample. An additional 4 percent was observed considering less-specific antibodies (31 women). Only 39 percent of sero-positive women accepted duodenal biopsy. HLA and biopsy data discarded celiac in 14 sero-positive cases (37 percent), only one with anti-TG2 antibodies. Celiac was suggested in 10 sero-positive and 3 sero-negative women (1.9 percent). Compared with controls, the live birthrate of the studied women with probable celiac was significantly decreased before removing gluten from the diet (P = .015), but significantly increased after that (P = .020).

In conclusion, at least one percent of celiac prevalence should be expected after serological screening of women with recurrent miscarriages. More importantly, the data clearly demonstrate that strict compliance with the gluten-free diet can significantly benefit the reproductive outcomes in women with celiac and gluten intolerance.

Exploring undiagnosed celiac disease in women with recurrent reproductive failure: The gluten-free diet could improve reproductive outcomes. *American Journal of Reproductive Immunology.* 2019 Nov 10:e13209. Alecsandru, D., López-Palacios, N., et al.

What are the most common autoimmune diseases associated with celiac disease?

It is well recognized that celiac disease and gluten intolerance are associated with increased risk of other autoimmune diseases. A new study has analyzed the scope of autoimmune diseases in patients with celiac.

The study included 230 celiac patients who were diagnosed and followed-up on between 2015-2019. All autoimmune diseases that accompanied celiac were recorded, and their association with risk factors was analyzed.

The mean age of the patients was 35.6 ±10.6 years (age range:18-72). A total of 58 patients (25.2 percent) were male and the mean age at onset of disease was 29.1±6.5 years. The duration of disease follow-up was 6.5±4.6 years. A total of 122 patients (53 percent) were on a strict diet, and 72 patients (31.3 percent) had accompanying autoimmune disease. Hashimoto's thyroiditis was found in 39 patients (17 percent) and asthma in 16 patients (7 percent) as the most common comorbidities.

Accompanying Autoimmune Diseases in Celiac Patients

	N - (%)		N - (%)
Dermatitis Herpetiformis	8 (3.5%)	Rheumatoid arthritis	2 (0.9%)
Type 1 Diabetes Mellitus	10 (4.3%)	Asthma	16 (7%)
Hashimoto's Thyroiditis	39 (17%)	Immune Thrombocytopenia	3 (1.3%)
Graves' Disease	2 (0.9%)	Hypogonadism	1 (0.45%)
Primer Biliary Cirrhosis	2 (0.9%)	Sjogren	6 (2.6%)
Autoimmune Hepatitis	8 (3.5%)	Psoriasis	2 (0.9%)
Systemic Lupus Erythematosus	1 (0.45%)	Autoimmune Hypoparathyroidism	4 (1.7%)
Scleroderma	2 (0.9%)	Dermatomyositis	2 (0.9%)
Familial Mediterranean Fever	2 (0.9%)	Gout Disease	1 (0.45%)
Behcet's Disease	2 (0.9%)	Ankylosing Spondylitis	1 (0.45%)

N: Number of patients.

There was a significant relation between autoimmune disease and female gender, age of diagnosis being <40 years, duration of disease, and non-GI symptoms at the time of admission.

In conclusion, the high prevalence of autoimmune disease among patients with celiac justifies the broad screening of celiac patients for associated autoimmune disorders.

Association of autoimmune diseases with celiac disease and its risk factors. *Pakistan Journal of Medical Sciences.* 2019 Nov-Dec; 35(6): 1548-1553. Kayar, Y., Dertli, R.

What is the mechanism of 'leaky gut syndrome' in patients with celiac disease?

Impaired intestinal permeability, also known as 'leaky gut syndrome,' is a frequent problem in patients suffering from celiac disease and gluten intolerance. However, the mechanism underlying this effect is not fully understood.

The aim of the current study was to evaluate the role of monocytes (a type of white blood cell) in eliciting the epithelial barrier defect in celiac patients. For this purpose, human monocytes were isolated from peripheral blood mononuclear cells (PBMCs) from active and inactive celiac patients and healthy controls. PBMCs were sorted for expression of CD14 (cell surface monocyte marker) and co-cultured with intestinal epithelial cells. Barrier function, as well as tight junctional alterations, were determined. In line with this, tight junctional alterations were found by confocal laser scanning microscopy and Western blotting of ZO-1, occludin, and claudin-5. Analysis of cytokine concentrations in monocyte supernatants revealed higher expression of interleukin-6 and MCP-1 in celiac monocytes. Celiac peripheral monocytes reveal an intrinsically elevated pro-inflammatory cytokine pattern that is associated with the potential of peripheral monocytes to affect barrier function by altering tight junction composition.

The conclusion of the study is that monocytes from patients with celiac can negatively affect intestinal barrier permeability and cause 'leaky gut syndrome.'

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Celiac disease monocytes induce a barrier defect in intestinal epithelial cells. *International Journal of Molecular Sciences*. 2019 Nov 9; 20(22). pii: E5597. Delbue, D., Cardoso-Silva, D., et al. SGF

As always, consult a medical professional before beginning any new protocol.

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***Dr. Alexander Shikhman**, founder of the Institute for Specialized Medicine, is board certified in internal medicine and rheumatology. Dr. Shikhman also launched Gluten-Free Remedies™, a line of all natural supplements which help treat the complications that can arise from celiac disease. Find Dr. Shikhman at **ifsmed.com** and **glutenfreeremedies.com**.*