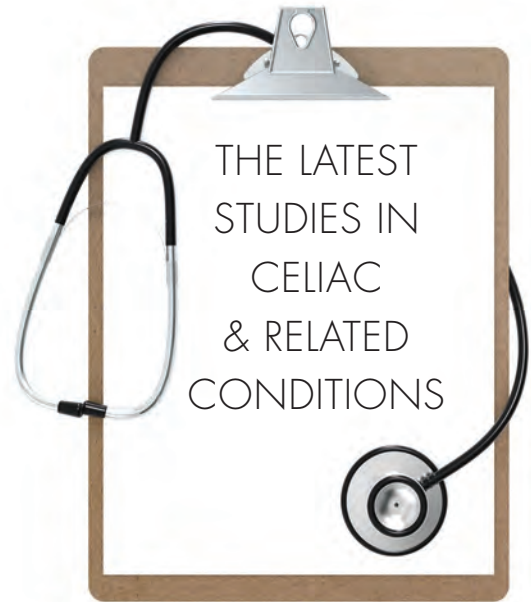


Research Roundup

Research publications on celiac disease, gluten sensitivity, and gluten-associated ailments grow every year with accelerated speed and it is getting more and more difficult to navigate the ocean of new data.

Therefore, we decided to commentate on some of the new trends and developments in this area. As a rheumatologist, the selection of articles reflects, to a certain degree, the scope of our medical practice.

Let's get started.



Can we predict whether a child with a celiac-prone genotype will develop celiac disease? The newest data tells us – yes, it is possible.

Celiac disease is a multifactorial disease influenced by both genetic and environmental risk factors. The genetic components are mainly due to HLA class II genes, which account for approximately 40 percent of the disease heritability. The environmental factor is linked to gliadin/gluten ingestion.

The lipid profile of infants has been proposed as a potential biomarker of celiac that can be measured before they exhibit developmental disorders and clinical symptoms.

Long before any exposure to gluten or any production of specific antibodies, several molecular mechanisms are significantly expressed in infants who will develop celiac, compared to their peers matched for the same genetic profile.

The present study explored the serum phospholipid profile of a group of infants at risk for celiac disease, followed up to 8 years to monitor the onset of celiac. Researchers compared 30 patients who developed the disease with 20 age- and sex-matched peers

with similar genetic profiles who did not develop the disease within 8 years.

Serum phospholipids were analyzed at 4 months, before exposure to gluten, and at 12 months of age, when none showed any marker of disease. In the 30 celiac patients, they also analyzed the serum at the time of diagnosis (>24 months).

The phospholipid signature was dramatically different in infants who developed celiac when compared to that of control NY-CeD (Not Yet developing Celiac Disease) peers.

Researchers identified a specific serum phospholipid signature that predicts the onset of celiac disease in HLA at-risk infants, years before the appearance of antibodies specific for celiac and before any clinical symptoms, even before gluten introduction into the diet at 4 months.

Although the full panel is not commercially available yet, the separate analytes can be tested via different laboratories.

A Phospholipid Profile at 4 Months Predicts the Onset of Celiac Disease in at-Risk Infants. Sci Rep. 2019 Oct 4;9(1):14303. Auricchio, R., Galatola, M., Cielo, D., et al.

The majority of symptomatic patients with diagnosed celiac disease and gluten sensitivity are very compliant with a gluten-free diet. When following a gluten-free diet, what are the most common nutrients that need to be supplemented?

Often, micronutrient deficiencies cannot be detected when a patient is already following a long-term gluten-free diet with good compliance. The aim of this narrative review is to evaluate the most recent literature that considers blood micronutrient deficiencies in compliant subjects, in order to prepare dietary supplementation advice (DSA).

This review included 73 studies. The few studies on micronutrient circulating levels in long-term gluten-free diet patients over 2 years with good compliance demonstrated that deficiency was detected in up to:

- 30 percent of subjects for vitamin B12 (DSA: 1,000 mcg/day until level is normal, then 500 mcg).
- 40 percent for iron (DSA: 325 mg/day).
- 20 percent for folic acid (DSA: 1 mg/day for 3 months, followed by 400-800 mcg/day).
- 25 percent for vitamin D (DSA: 1,000 IU/day or more based on serum level or 50,000 IU/week if level is <20 ng/mL).
- 40 percent for zinc (DSA: 25-40 mg/day).
- 3.6 percent of children for calcium (DSA: 1,000-1,500 mg/day).
- 20 percent of children for magnesium (DSA: 200-300 mg/day).

In conclusion, if proper diet is not enough, supplementation may be needed after evaluating the initial blood level to determine the right dosage.

Our recommendation is for people on a gluten-free diet to be tested annually for nutritional profile/micronutrients. The test is commercially available via different laboratories.

Micronutrients Dietary Supplementation Advice for Celiac Patients on Long-Term Gluten-Free Diet with Good Compliance: A Review.

Medicina 2019, 55, 337. Rondanelli, M., Faliva, MA., Gasparri, C., et al.

Existing data demonstrates a growing correlation between nonalcoholic fatty liver and celiac disease.

Nonalcoholic fatty liver disease is a growing condition among adolescent and adult populations, present in around 20-30 percent of people in the United Kingdom. In the future, it may become a leading contributor to cirrhosis, liver transplantation, and mortality.

A gluten-free diet is known to be associated with altered macronutrient intake and metabolic syndrome. Nonalcoholic fatty liver disease (NAFLD) is the liver hallmark of metabolic syndrome.

Patients were matched for demographic characteristics (age and gender) and metabolic risk factors (overweight, diabetes mellitus, total cholesterol, and triglycerides) using a 1:1 ratio. NAFLD was diagnosed according to the European Association for the Study of the Liver criteria.

The study compared 202 celiac disease patients and 202 controls. The raw prevalence of NAFLD was 34.7 percent and 21.8 percent in the celiac and control group, respectively ($P = 0.006$). Binary logistic regression confirmed an increased risk of NAFLD in the celiac group (adjusted odds ratio = 2.90, 95 percent confidence interval: 1.64-5.15,

$P < 0.001$). Additionally, the relative risk for NAFLD was notably higher in non-overweight celiac patients (adjusted odds ratio = 5.71, 95% confidence interval: 2.30-14.19, $P < 0.001$).

More than one-third of celiac patients adhering to a gluten-free diet had concurrent NAFLD, accounting for a three-fold increased risk compared to the general population. Dietary advice using a patient-tailored approach should assist celiac patients with NAFLD in achieving an appropriate nutritional intake whilst reducing the risk of long-term liver-related events.

People with celiac disease need to be evaluated for NAFLD. If the diagnosis is positive, the disease can be effectively treated using dietary modifications combined with drugs and/or food supplements.

Increased risk of nonalcoholic fatty liver disease in patients with coeliac disease on a gluten-free diet: beyond traditional metabolic factors. Aliment Pharmacol Ther. 2018 Sep;48(5):538-546. Tovoli, F., Negrini, G., Fari, R., et al.

Autoimmune thyroid diseases, including Hashimoto's thyroiditis and Graves' disease, frequently coexist with celiac disease and non-celiac gluten sensitivity. A recent study addressed the issue of whether a gluten-free diet may benefit thyroid autoimmunity in drug-naïve patients (not taking drugs for treatment).

The purpose of this study was to investigate whether a gluten-free diet affects thyroid autoimmunity, hypothalamic-pituitary-thyroid axis activity, and thyroid function tests in women with Hashimoto's thyroiditis and incidentally found positive anti-tissue transglutaminase antibodies.

The study included 34 women with autoimmune thyroiditis divided into two groups. The patients belonging to the first one (group A, n=16) complied with the gluten-free diet for 6 months, while the remaining


patients (group B, n=18) remained without any dietary treatment.

Serum titers of thyroid peroxidase and thyroglobulin antibodies, as well as serum levels of thyrotropin, free thyroid hormones, and 25-hydroxyvitamin D were measured at the beginning of the study and 6 months later.

In group B, serum thyrotropin, free thyroid hormones, and serum 25-hydroxyvitamin D remained at similar levels.

In group A, the impact on thyroid autoantigens (TPOAb and TgAb) titers correlated with the changes in the thyroid output (SPINA-GT index), whereas the impact on TPOAb correlated with the changes in 25-hydroxyvitamin D levels. The gluten-free diet reduced thyroid antibody titers, as well as slightly increased 25-hydroxyvitamin D levels.

The obtained results suggest that the gluten-free diet may bring clinical benefits to women with autoimmune thyroid disease by stabilizing thyroid function in these women. The exact mechanism of this phenomenon is to be discovered.

The Effect of Gluten-Free Diet on Thyroid Autoimmunity in Drug-Naïve Women with Hashimoto's Thyroiditis: A Pilot Study. Exp Clin Endocrinol Diabetes. 2019 Jul;127(7):417-422. Krysiak, R., Szkróbka, W., Okopień, B. 

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



ABOUT THE AUTHOR:
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 ifsmmed.com and glutenfreeremedies.com.