

January 01/08: IgG in CD patients with IgA deficiency

Coeliac disease (CD), characterised by intolerance to dietary gluten-intake, affects up to 1% of the European population. Diagnosis still relies on a suggestive jejunal biopsy result, but it has been shown that the presence of IgA antibodies to tissue transglutaminase (tTG) can be used as a sensitive and specific initial serological screen for coeliac disease.

Selective IgA deficiency (SIgAD) occurs in the normal population with a prevalence of 1:300 to 1:800. It is a heritable condition in which total serum IgA level is below 0.05 g/l with IgM and IgG serum levels remaining within normal ranges. Clinical studies show an increased prevalence of selective IgA deficiency in celiac disease patients (3-10% of all CD patients). The diagnosis of CD in IgA deficient subjects is a special challenge since the classical IgA markers are not produced. IgG class assays using recombinant human tTG as antigen have proven to be highly reliable serological tests for the diagnosis of CD in patients with SIgAD.

The authors of the following article conducted a comparative study of nine methods used for measuring anti-tTG IgG antibodies in patients with CD and SIgAD:

Villalta D, Alessio MG, Tampola M, Tonutti E, Brusca I, Bagnasco M, Pesce G, Stella S, Bizzaro N
Testing for IgG class antibodies in celiac disease patients with selective IgA deficiency. A comparison of the diagnostic accuracy of 9 IgG anti-tissue transglutaminase, 1 IgG anti-gliadin and 1 IgG anti-deamidated gliadin peptide antibody assays
Clin Chim Acta 2007, 382: 95-99

20 consecutive CD patients with IgA deficiency, diagnosed according to the revised ESPGHAN criteria and not on a gluten-free diet, and 113 controls were measured for anti-tTG IgG antibodies using 9 different commercial methods: 6 using recombinant human tTG as antigen, 1 using native human tTG, 1 using recombinant tTG cross-linked with gliadin-specific peptides and 1 using purified human endomysial antigen and gliadin fragments. Sensitivity and specificity for each kit were calculated both using the manufacturers' cutoff and the optimal decision threshold obtained by ROC curves analysis. All sera were also tested for anti-Gliadin IgG by a commercial ELISA and by a test using a preparation of purified deamidated gliadin peptides as antigen (IgG anti-DGP from Inova).

	Aesku	D-tek	Euro-immun	Phadia	Generic Assays	Immco	Inova	Orgentec	Radim	IgG anti-Gliadin	
	Rh-tTG+ *	Rh-tTG	Rh-tTG	Rh-tTG	Rh-tTG+ **	Rh-tTG	Nh-tTG	Rh-tTG	Rh-tTG	Radim	Inova
Antigen	Rh-tTG+ *	Rh-tTG	Rh-tTG	Rh-tTG	Rh-tTG+ **	Rh-tTG	Nh-tTG	Rh-tTG	Rh-tTG	Gliadin	anti-DGP
Sens %	85	75	80	95	95	95	75	95	95	40	80
Spec %	95	97	100	100	91	91	99	94	88	87	98

Table: Diagnostic sensitivity and specificity of 9 tTG IgG assays, 1 anti-gliadin IgG assay and 1 assay for anti-deamidated gliadin peptides IgG. For details see table 2 on page 97 of the original article.

* Rh-tTG X-linked with gliadin peptides

** Rh-tTG + gliadin fragments

The authors conclude that all IgG anti-tTG methods evaluated are reliable serologic assays (when cut-offs are appropriately set) for the diagnosis of CD in patients with IgA deficiency and perform better than the gliadin-based assays used in this study. The tests containing both tTG and gliadin peptides are burdened by a lower specificity than the anti-tTG assays. Remarkably, the assay based on deamidated gliadin peptides showed a much lower sensitivity and also a slightly lower specificity than the best anti-tTG assay.

