Revista Española de Enfermedades Digestivas
The Spanish Journal of Gastroenterology

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DOI: 10.17235/reed.2024.10791/2024
Link: PubMed (Epub ahead of print)

Please cite this article as:
Pascual Lorén María, Martín-Adrados Ana, González Cervera Rosa María , Martínez Pérez Jorge , Quintero García Ana Isabel , Muñoz Codoceo Rosa Ana. Validation of a rapid test for celiac disease detection in first-degree relatives — A prospective study. Rev Esp Enferm Dig 2024. doi: 10.17235/reed.2024.10791/2024.

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CC 10791

Validation of a rapid test for celiac disease detection in first-degree relatives — A prospective study

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Authors´ contribution: Methodology: R. M. G. C., and J. M. P.; project administration: M. P. L.; supervision: A. I. Q. G., and R. A. M. C.; writing-review and editing: A. M. A.

Conflict of interest: the authors declare no conflict of interest.

Artificial intelligence: the authors declare that they did not use artificial intelligence (AI) or any AI-assisted technologies in the elaboration of the article.

Keywords: Celiac disease. Rapid test.

Dear Editor,

Celiac disease (CD) is an autoimmune condition triggered by gluten in genetically susceptible individuals. Based on the European Society for Pediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) 2020 guidelines, the primary diagnosis of CD relies on the detection of anti-tissue transglutaminase type 2 antibodies (anti-tTG2) in serum (1).

As it is a human leukocyte antigen (HLA) dependent condition, first-degree relatives (FDRs) of celiac patients are at higher risk than the general population of developing

CD. A meta-analysis which compared 54 articles showed that the pooled prevalence of CD was 7.5 % among FDRs and 2.3 % among second-degree relatives compared to 1.4 % in the general population (2). This population may be asymptomatic or present very mild symptoms, manifesting in silent, latent, or potential forms of the disease. Despite the absence of symptoms, diagnosis is essential to start a gluten-free diet and prevent complications associated with nutrient malabsorption and immune system dysfunction.

The study presented here aimed to validate CeliacDetect (Biomedal S.L., Seville, Spain), a new rapid diagnosis test for CD. It is a lateral flow immunoassay (LFIA) for outpatient use, which allows the detection of anti-tTG2 IgA antibodies in capillary blood samples, obtaining a result in ten minutes. This test can be performed in the daily practice at the medical clinic as it is easy and minimally invasive. The first step is to clean and massage the fingertip with an alcohol pad and then puncture it using an automatic lancet. A blood drop is collected in the glass capillary tube. Once the tube, approximately 2 cm in length, is filled, it is placed into a buffer bottle and mixed by inversion. Finally, five drops of this mixture are applied to the LFIA.

A qualitative result is given. If the sample contains anti-tTG2 antibodies, a red line appears (positive result), which indicates the possibility of suffering from CD, considering anti-tTG2 > 5 U/ml as positive. The absence of this line (negative result) confirms that the blood sample does not contain anti-tTG2 antibodies within the detection limits of the kit and, therefore, implies a low suspicion of CD.

A prospective, single-center study was coordinated between the Clinical Analysis Laboratory and the Gastroenterology Department from March 2023 to March 2024. Informed consent was obtained from all patients over 12 years old and parents or legal guardians of subjects involved in the study who were under 12 years of age. First-degree relatives of CD patients were tested *in situ,* performing the CeliacDetect rapid test and comparing it with the routine laboratory technique (serum anti-tTG2 determination along with total IgA levels).

For this purpose, the IDS t-TG IgA diagnostic kit was used, a chemiluminescence immunoassay (CLIA) for the quantitative determination of IgA-specific antibodies directed against tissue anti-transglutaminase (t-TG) in human serum or plasma

samples. A sample was considered as positive if it presented titers higher than 10 IU/ml. This posed a limitation because there is a gray area between the positive result of the CeliacDetect test (> 5 IU/ml) and the positive result of the laboratory technique. Previously diagnosed CD cases or those with IgA deficiency were excluded.

The study included 95 participants, who were FDRs of CD patients: 27 (28 %) mothers, 27 (28 %) fathers, and 41 (43 %) siblings of diagnosed CD patients. Five potential participants were excluded, two because they did not undergo the laboratory sample extraction, and three with IgA deficiency. Eight patients (8.8 %) tested positive in the rapid test and all of them (100 %) were subsequently confirmed to have CD with values of anti-tTG2 > 100 U/ml by the routine laboratory technique. All were siblings of CD patients, aged between two and 15 years. The remaining patients (91 %) were negative for both determinations (Table 1).

This appears to be a very positive result in terms of accuracy, as both sensitivity and specificity were 100 %, as well as the positive and negative predictive values. In addition to evaluating the sensitivity and specificity of the test, a ROC curve (Fig. 1) analysis was also performed to assess its discriminative ability. The ROC curve showed an area under the curve (AUC) of 1, indicating a high level of accuracy in the test's ability to distinguish between patients with and without CD.

In this same line of CD research, there have been few other publications that advocate the use of this rapid tests for screening (3,4), which is simple and quick to use in a typical medical consultation. When comparing the results obtained, the test used in this study is one of the most accurate (PPV 100 %), which would translate to a reduction in the number of people sent for additional laboratory tests resulting in a decrease in costs, risk, and refusals of diagnosis.

These results further support the utility of the rapid test as an effective tool for screening CD in relatives of diagnosed patients. However, it would be important to perform more studies with a large sample size. As IgA antibodies are detected, having an IgA deficiency is an evident limitation of the use of this test.

As recommended in the latest clinical practice guidelines, screening based on genetic risk should be performed (5). We propose that at the time of diagnosing a celiac patient, a blood test with HLA determination should be performed on his/her siblings,

to assess the risk and measure total IgA in the same sample. Based on the risk according to the HLA, monitoring can be performed, with the following determinations being carried out with the rapid CeliacDetect test once IgA deficiency has been ruled out.

This study provides the novelty of using a quick and easy test for screening. This finding could have a significant impact on clinical practice by enabling early and accessible detection of the disease in first-degree relatives, which may lead to timely intervention and improved quality of life of patients.

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Table 1. Results of the CeliacDetect rapid test compared to the results obtained with the laboratory reference test

	Reference test			
Rapid test (CeliacDetect)		**Positive**	**Negative**	**Total**
	Positive	8	0	8
	Negative	0	82	82
	Total	8	82	90

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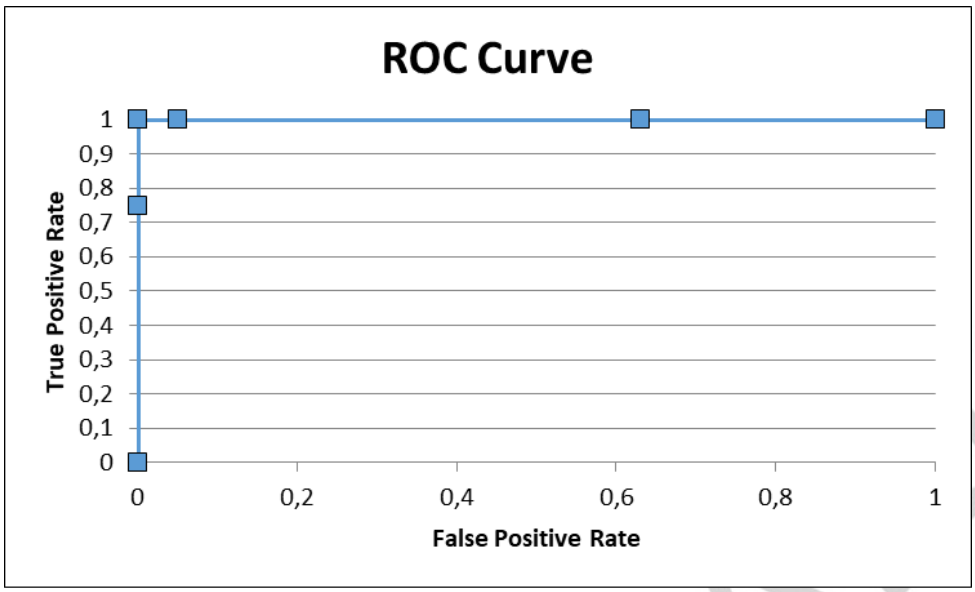

Fig. 1. ROC curve.