

Research Article

Beyond Anti-Ttg Antibodies: Diagnostic Value Of Antibodies Against Deamidated Gliadin Peptides In Celiac Disease.

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Abstract

Celiac disease is an autoimmune enteropathy whose diagnosis primarily relies on serological testing, with IgA anti-tissue transglutaminase (anti-tTG) antibodies serving as the first-line biomarker. However, their diagnostic performance may be limited in certain situations, particularly in cases of selective IgA deficiency or atypical clinical presentations. Antibodies directed against deamidated gliadin peptides (anti-DGP) represent a promising alternative, but their role in diagnostic strategies remains controversial. This study aimed to evaluate the diagnostic performance of anti-tTG and anti-DGP antibodies, used alone or in combination, in Moroccan patients with celiac disease. This retrospective single-center study included 96 serum samples from 49 patients with confirmed celiac disease and 47 healthy controls. IgA and IgG anti-tTG antibodies, as well as IgA and IgG anti-DGP antibodies, were detected using the immunodot technique. Serological profiles were compared between the two groups using Pearson's χ^2 test. A total of 96 participants were included, comprising 49 patients with confirmed celiac disease and 47 healthy controls. Among the patients, 65% were children and 35% were adults, with a female predominance (63%; sex-ratio = 0.58). In contrast, the control group consisted predominantly of adults (59%) and showed a balanced sex distribution (51% male). All controls were seronegative for the four biomarkers investigated. Among patients, positivity rates were 59.2% for IgA anti-tTG, 46.9% for IgA anti-DGP, 40.8% for IgG anti-tTG, and 49.0% for IgG anti-DGP ($p < 0.0001$). Combined analysis of serological profiles showed that 87.8% of patients had at least one IgA autoantibody, compared with 61.2% for IgG autoantibodies. Isolated anti-DGP positivity was observed in 28.6% of patients for IgA and 20.4% for IgG, highlighting the complementary value of these biomarkers relative to anti-tTG antibodies and suggesting that a multi-marker serological approach could improve the detection of celiac disease cases with heterogeneous immunological profiles. The combined use of anti-tTG and anti-DGP antibodies improves the serological detection of celiac disease compared with an approach based on a single biomarker. Although IgA anti-tTG remains the first-line reference test, IgG anti-DGP provides additional diagnostic value, particularly in atypical cases or when clinical suspicion persists. These findings, obtained from a Moroccan population, support the value of a multi-marker serological strategy adapted to settings where diagnostic resources are limited and warrant confirmation through prospective multicenter studies.

Keywords: Celiac disease; Serological diagnosis; Anti-tissue transglutaminase antibodies; Deamidated gliadin peptide antibodies; Diagnostic performance.

INTRODUCTION

Celiac disease is a chronic autoimmune disorder triggered by gluten exposure in genetically predisposed individuals. Genetic susceptibility is strongly associated with the presence of the HLA-DQ2 and/or HLA-DQ8 haplotypes, which are found in more than 95% of affected patients. However, these haplotypes are not disease-specific, as they are also present in a substantial proportion of the general population, thereby limiting their positive diagnostic value, whereas their absence has an excellent negative predictive value [1,2]. The disease

is characterized by an abnormal immune response directed against the small intestinal mucosa, resulting in chronic inflammation and varying degrees of villous atrophy. Its prevalence is estimated at approximately 1% of the global population. However, this figure is likely underestimated because of the high frequency of asymptomatic, atypical, or oligosymptomatic forms, which contribute to considerable diagnostic delay. Historically, the diagnosis has relied on the integration of clinical, serological, and histological findings. According to the most recent recommendations of the European Society for Pediatric Gastroenterology, Hepatology

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and Nutrition (ESPGHAN, 2020) and the American College of Gastroenterology (ACG, 2023), a biopsy-sparing diagnostic approach may be considered in well-defined situations, particularly in children with IgA anti-tissue transglutaminase antibody (IgA anti-tTG) levels exceeding ten times the upper limit of normal, provided that strict diagnostic criteria are fulfilled [1,2].

Serological testing currently represents the cornerstone of celiac disease screening and diagnosis. Among the available biomarkers, IgA antibodies against tissue transglutaminase (IgA anti-tTG) are recommended as the first-line test by most international guidelines because of their excellent diagnostic performance, with sensitivity and specificity generally ranging from 90% to 98%, depending on the analytical method used. International recommendations also advocate the routine measurement of total serum IgA levels to identify selective IgA deficiency, which may lead to false-negative IgA-based serological results and therefore warrants the use of IgG-based markers [3–6]. Nevertheless, this approach has certain limitations in specific clinical settings, particularly in patients with selective IgA deficiency, which is observed in approximately 2–3% of individuals with celiac disease, in children younger than two years of age, or in cases with a strong clinical suspicion despite negative serology. In these situations, additional biomarkers, especially IgG antibodies against deamidated gliadin peptides (IgG anti-DGP) as well as IgG anti-tTG antibodies, may improve diagnostic performance [3–6]. Several recent studies have confirmed the diagnostic value of IgG anti-DGP antibodies. Their sensitivity ranges from 74% to 88% across studies and may reach 100% in certain pediatric cohorts, whereas their specificity generally ranges between 96% and 99%. In young children and in patients with IgA deficiency, these antibodies may even demonstrate superior diagnostic performance compared with IgA anti-tTG antibodies [1,3–6].

Furthermore, combining multiple serological markers, particularly IgA anti-tTG and IgG anti-DGP antibodies, has been shown to improve screening sensitivity, especially in mild or oligosymptomatic forms of the disease, while maintaining satisfactory specificity when appropriate decision thresholds are applied. A recent study demonstrated that concomitant positivity for IgA anti-tTG and IgG anti-DGP antibodies, with titers exceeding ten times the upper limit of normal, was associated with a positive predictive value of 100% for Marsh type 3 histological lesions, thereby supporting the feasibility of a biopsy-free diagnosis in such cases. Conversely, some authors have reported that the systematic inclusion of anti-DGP antibodies in serological panels may reduce specificity when positivity thresholds are not adequately optimized. Moreover, isolated IgG anti-DGP positivity in patients with a low pretest probability leads to a confirmed diagnosis of celiac disease in only a limited proportion of cases, approximately 15% [1,3–5].

In Morocco, as in other North African countries, data regarding the epidemiology of celiac disease and the comparative performance of the different serological assays remain limited. This situation is mainly attributable to heterogeneity in diagnostic practices, unequal access to specialized laboratory techniques, and the lack of robust local data. In this context, evaluating the diagnostic performance of the main available serological biomarkers, including IgA and IgG anti-tTG as well as IgA and IgG anti-DGP antibodies, is essential to optimize diagnostic strategies according to the characteristics of the Moroccan population [7].

Despite the regular updates of international guidelines, the exact role of IgG anti-DGP antibodies and the added value of a comprehensive serological panel combining IgA/IgG anti-tTG and IgA/IgG anti-DGP antibodies remain a matter of debate, particularly in countries with limited resources or intermediate disease prevalence. Specifically, it remains to be determined whether this combined strategy significantly improves screening sensitivity without compromising specificity while maintaining clinical relevance in populations with limited diagnostic resources.

Against this background, the aim of the present study was to evaluate the diagnostic performance of IgA and IgG anti-tTG antibodies as well as IgA and IgG anti-DGP antibodies in the screening of celiac disease. We also compared different serological strategies, including the combination of IgA anti-tTG and IgG anti-DGP antibodies and the complete IgA/IgG anti-tTG plus IgA/IgG anti-DGP panel, with IgA anti-tTG testing alone, in order to assess their additional diagnostic value and clinical relevance in a Moroccan population.

PATIENTS AND METHODS

Ethical Considerations

This retrospective study was conducted using archived serum samples and anonymized clinical and biological data, in accordance with the ethical principles of the Declaration of Helsinki and applicable confidentiality regulations. Samples and data were used exclusively for research purposes, and no personally identifiable information was accessible to the investigators (**Figure 1**).

Patients

This retrospective single-center study was conducted using archived serum samples from the serum biobank of the Immunology Laboratory, Faculty of Medicine and Pharmacy of Casablanca. A total of 96 serum samples were included, comprising 49 patients with confirmed celiac disease and 47 healthy controls.

Patients were eligible if they had a confirmed diagnosis of celiac disease, an available serum sample collected at the time of diagnosis before the initiation of a gluten-free diet,

and a sufficient serum volume for the measurement of IgA and IgG anti-tTG as well as IgA and IgG anti-DGP. Patients who had initiated a gluten-free diet before serum collection, those with hemolyzed samples, inadequate analytical sample quality, or insufficient serum volume, and patients whose clinical or laboratory data were insufficient to confirm the diagnosis were excluded.

The control group consisted of healthy individuals with no history or clinical manifestations suggestive of celiac disease. Individuals with conditions that could influence serological test results, including autoimmune diseases, chronic gastrointestinal disorders, or adherence to a gluten-free diet, were excluded (Figure 1).

METHODS

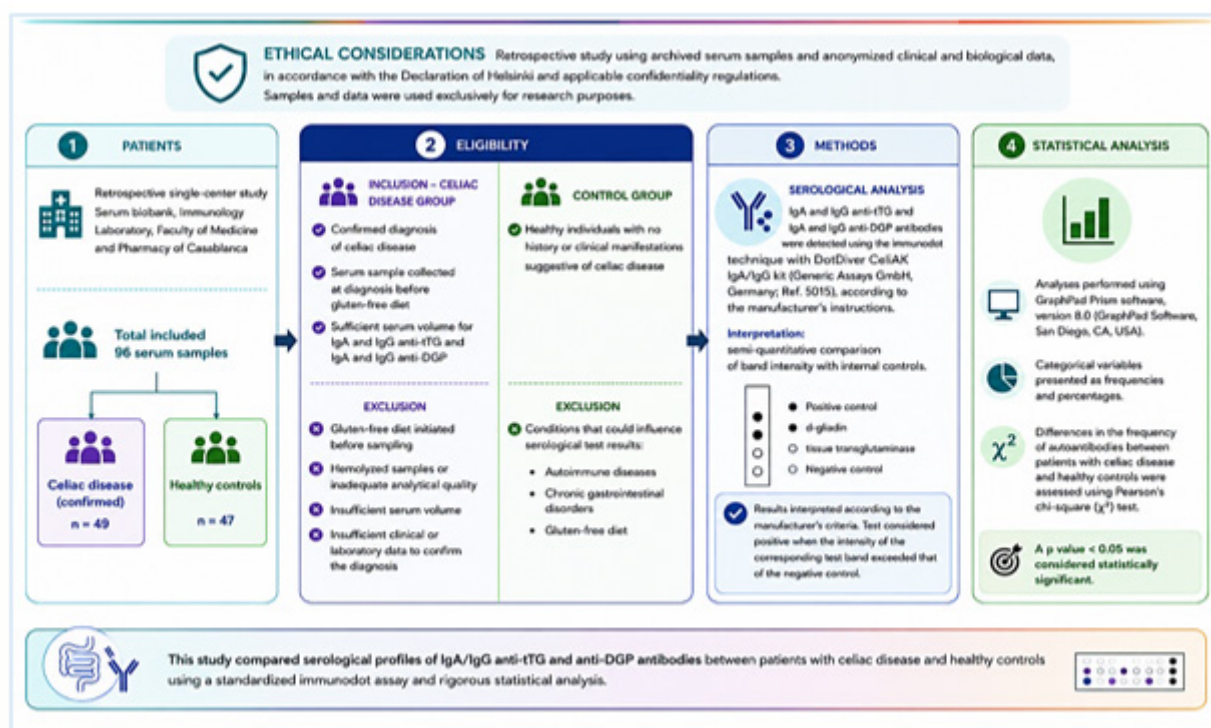
Serological Analysis

IgA and IgG anti-tTG antibodies, as well as IgA and IgG anti-DGP antibodies, were detected using the immunodot technique with the commercially available DotDriver CeliAK IgA/IgG kit (Generic Assays GmbH, Germany; Ref. 5015), according to the manufacturer's instructions. This assay is based on the simultaneous detection of multiple autoantibodies using specific antigens immobilized on a membrane. Serological profiles were interpreted semi-quantitatively by comparing the intensity of the immunoreactive bands with the internal controls provided in the kit. Results were interpreted according to the manufacturer's criteria, and a test was considered positive when the intensity of the corresponding test band exceeded that of the negative control (Figure 1).

Statistical Analysis

Statistical analyses were performed using GraphPad Prism software, version 8.0 (GraphPad Software, San Diego, CA, USA). Categorical variables are presented as frequencies and percentages. Differences in the frequency of autoantibodies between patients with celiac disease and healthy controls were assessed using Pearson's chi-square (χ^2) test. A p value < 0.05 was considered statistically significant (Figure 1).

Figure 1. Study Flow Chart.

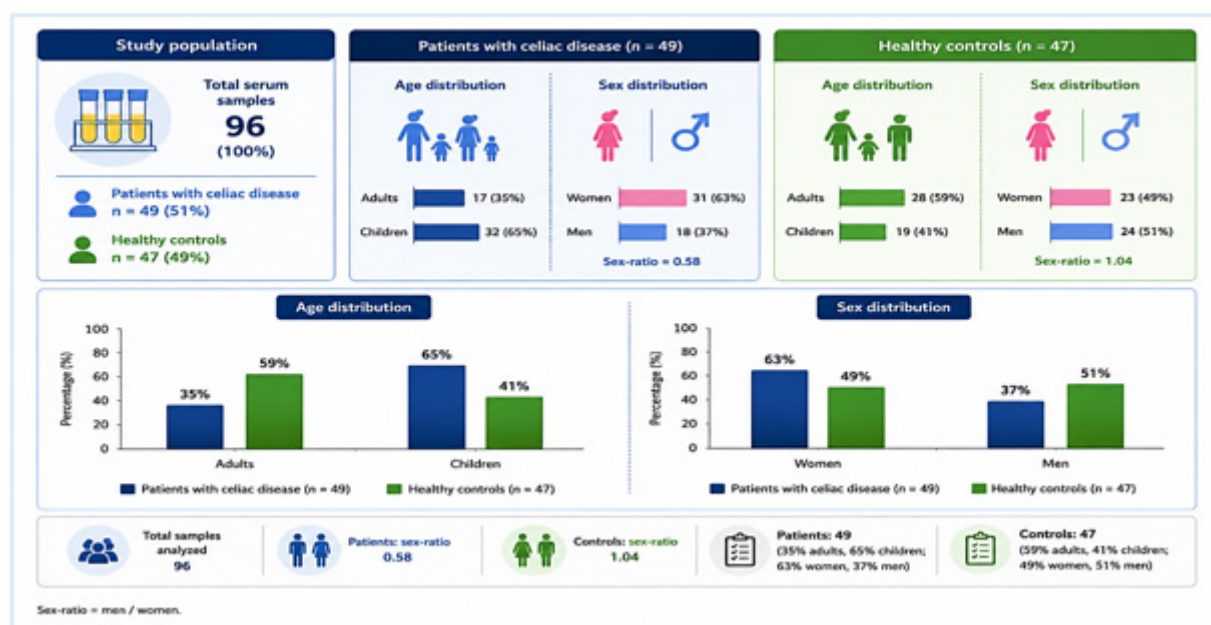


RESULTS

Demographic Characteristics of Patients and Controls

Figure 2 illustrates the demographic characteristics of the study participants. Among the 49 patients with celiac disease, 65% were children and 35% were adults. In contrast, the control group comprised 59% adults and 41% children. A female predominance was observed among patients (63%; sex-ratio = 0.58), whereas the control group showed a nearly balanced sex distribution, with a slight male predominance (51%; sex-ratio = 1.04).

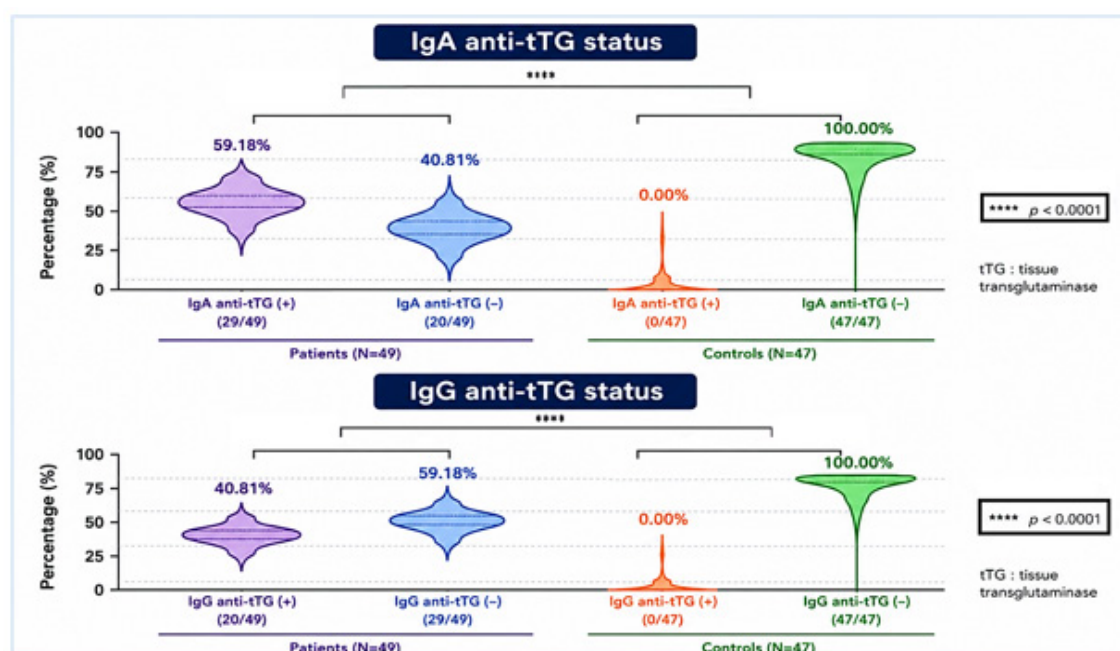
Figure 2. Distribution of patients and controls by age and sex.



Serological Status of IgA and IgG Anti-tTG Antibodies in Patients with Celiac Disease and Controls

Among patients with celiac disease (n = 49), 59.18% tested positive for IgA anti-tTG, while 40.81% tested positive for IgG anti-tTG. In contrast, none of the controls (n = 47) had detectable anti-tTG antibodies of either isotype, corresponding to a seronegativity rate of 100% in this group. The differences observed between patients and controls were statistically significant for both antibody isotypes ($p < 0.0001$) (Figure 3).

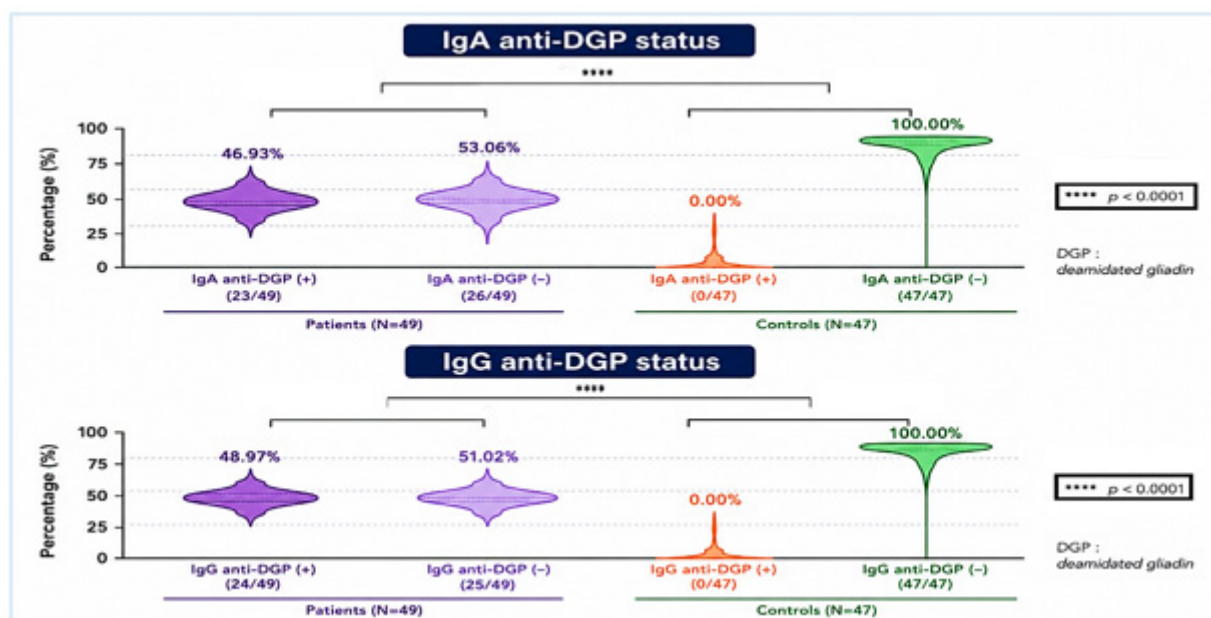
Figure 3. Seroprevalence of IgA and IgG anti-tTG in patients with celiac disease and healthy controls.



Serological Status of IgA and IgG Anti-DGP Antibodies in Patients with Celiac Disease and Controls

Among patients with celiac disease ($n = 49$), 46.93% tested positive IgA anti-DGP, while 48.97% tested positive for IgG anti-DGP. In contrast, none of the controls ($n = 47$) had detectable anti-DGP antibodies of either isotype, corresponding to a seronegativity rate of 100% in this group. The differences observed between patients and controls were statistically significant for both antibody isotypes ($p < 0.0001$) (Figure 4).

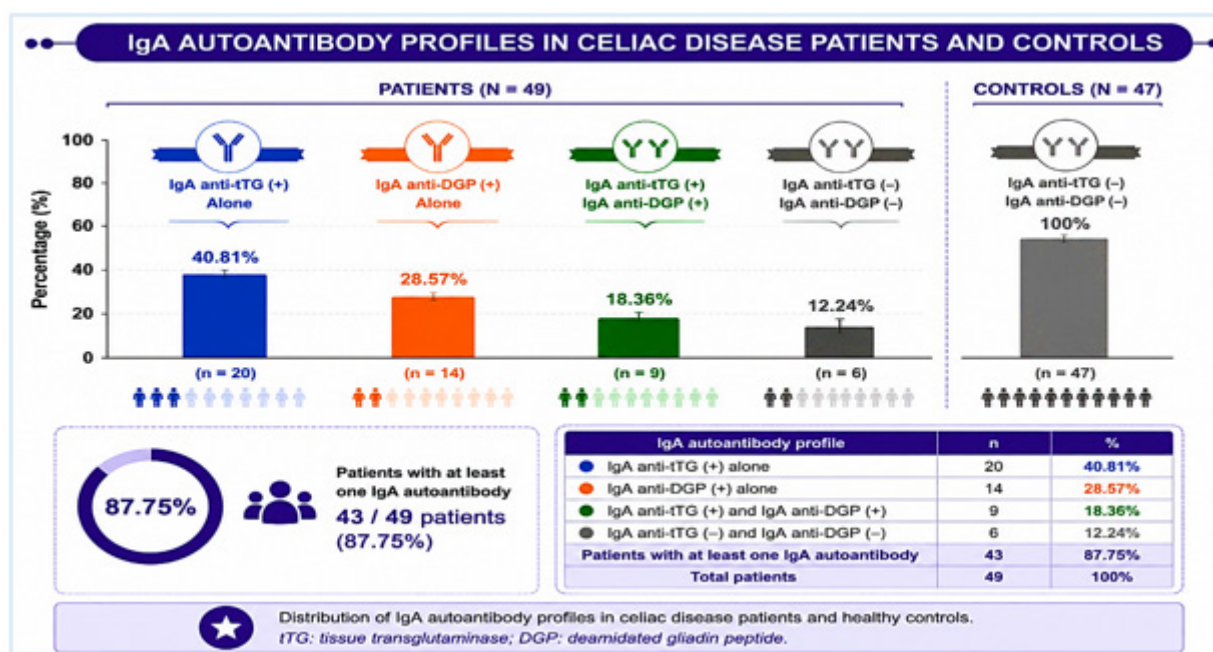
Figure 4. Seroprevalence of IgA and IgG anti-DGP in patients with celiac disease and healthy controls.



Serological Profiles of IgA Anti-tTG and IgA Anti-DGP Autoantibodies in Patients with Celiac Disease and Controls

Figure 5 illustrates the serological profiles of IgA anti-tTG and IgA anti-DGP in patients with celiac disease ($n = 49$) and healthy controls ($n = 47$). Among the patients, 43 (87.75%) tested positive for at least one of the two autoantibodies. Isolated IgA anti-tTG positivity was observed in 20 patients (40.81%), whereas 14 (28.57%) were positive only for IgA anti-DGP. Dual positivity for both IgA anti-tTG and IgA anti-DGP was detected in 9 patients (18.36%). Only 6 patients (12.24%) were negative for both markers. In contrast, none of the healthy controls (100%) tested positive for either autoantibody.

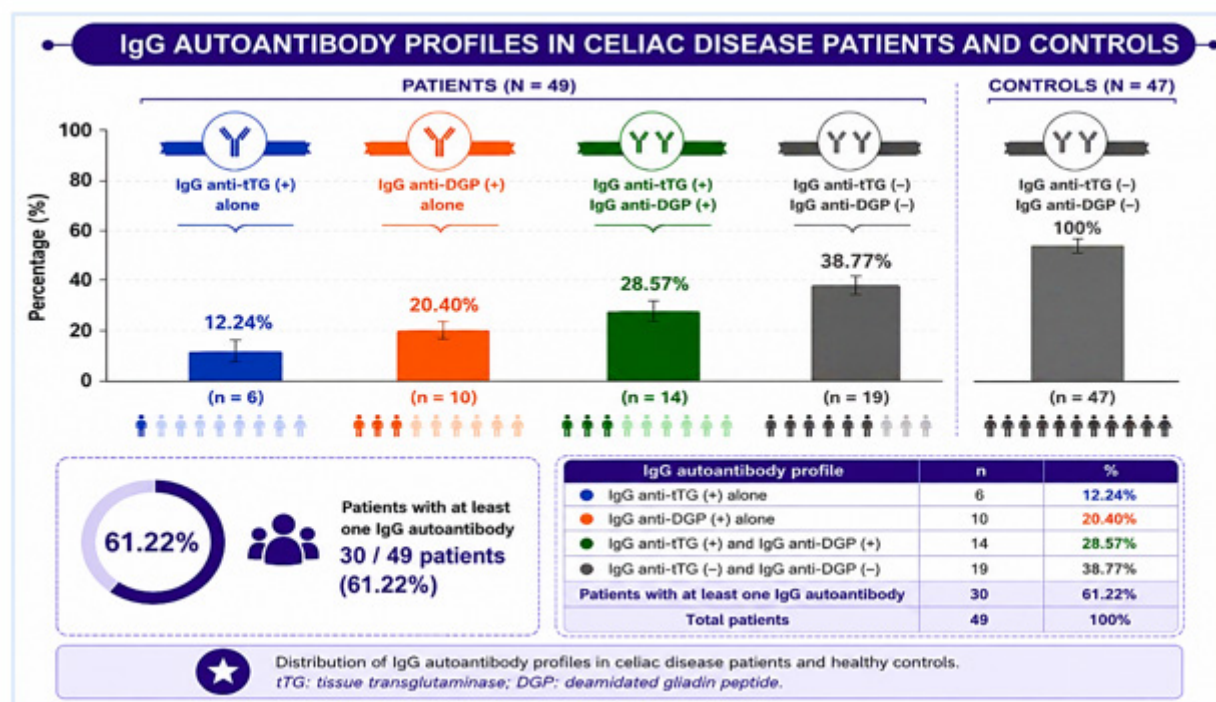
Figure 5. Seroprevalence of IgA anti-tTG and IgA anti-DGP in patients with celiac disease and healthy controls.



Serological Profiles of IgG Anti-tTG and IgG Anti-DGP Autoantibodies in Patients with Celiac Disease and Controls

Figure 6 illustrates the distribution of IgG anti-tTG and IgG anti-DGP serological profiles in patients with celiac disease ($n = 49$) and healthy controls ($n = 47$). Overall, 30 patients (61.22%) were positive for at least one IgG autoantibody. Isolated IgG anti-tTG and IgG anti-DGP positivity was observed in 6 (12.24%) and 10 (20.40%) patients, respectively, while 14 patients (28.57%) showed dual positivity for both autoantibodies. Nineteen patients (38.77%) were negative for both markers. All healthy controls (100%) were seronegative for both IgG anti-tTG and IgG anti-DGP.

Figure 6. Seroprevalence of IgA anti-tTG and IgA anti-DGP in patients with celiac disease and healthy controls.



DISCUSSION

Serological testing has become a cornerstone in the diagnosis of celiac disease, both for initial screening and for the implementation of currently recommended diagnostic strategies. The most recent international guidelines continue to recommend IgA anti-tissue transglutaminase antibodies (IgA anti-tTG) as the first-line serological test while recognizing the value of IgG antibodies against deamidated gliadin peptides (IgG anti-DGP) in specific clinical situations, particularly in patients with selective IgA deficiency, in young children, or when a strong clinical suspicion persists despite negative conventional serology. In this context, our findings provide original data from a Moroccan population, demonstrating that both anti-tTG and anti-DGP antibodies effectively discriminate patients with celiac disease from healthy controls and that their combined use may improve the diagnostic yield.

In our cohort, IgA anti-tTG antibodies were positive in 59.18% ($n = 29$) of patients with celiac disease, whereas no false-positive results were observed among healthy controls, indicating excellent diagnostic specificity within our study population (Figure 3). These findings are generally consistent

with the literature, which recognizes IgA anti-tTG as the first-line serological marker for the diagnosis of celiac disease because of its excellent sensitivity and specificity. However, the positivity rate observed in our study was lower than that commonly reported, where the sensitivity of IgA anti-tTG generally exceeds 90%. This discrepancy may be explained, at least in part, by methodological factors. Among the 49 serum samples obtained from patients with celiac disease, 20 yielded negative results by the immunodot assay. This discordance may be related to pre-analytical conditions, as serum samples had been stored frozen for approximately three months before analysis. Previous studies have shown that storage duration and conditions may affect antibody stability and consequently reduce the performance of subsequent immunological assays, particularly their sensitivity. Other factors reported in the literature that may account for such discrepancies include age younger than two years, selective IgA deficiency, low anti-tTG antibody concentrations, and inter-assay analytical variability. These findings highlight the limitations of relying on a single serological marker and support the use of a multimarker diagnostic approach, particularly in patients with persistent clinical suspicion despite an initially negative serological evaluation [9,10–12].

Our findings are also consistent with current recommendations, which state that IgG anti-tTG testing should not replace IgA anti-tTG but should instead be used as a complementary test in selected clinical settings, particularly in patients with selective IgA deficiency or when a strong clinical suspicion persists despite negative IgA serology. In our cohort, IgG anti-tTG antibodies were detected in 40.81% ($n = 20$) of patients with celiac disease (Figure 3). All patients who tested positive for IgG anti-tTG were also positive for IgA anti-tTG, whereas nine patients were positive exclusively for IgA anti-tTG. Consequently, IgG anti-tTG testing did not identify any additional cases in our series. This finding suggests that, in patients without known IgA deficiency, the additional diagnostic value of IgG anti-tTG is limited when used alongside IgA anti-tTG. Nevertheless, IgG anti-tTG remains clinically valuable in specific settings, particularly in patients with selective IgA deficiency, where it helps reduce the risk of false-negative results and complements the serological assessment.

One of the major findings of the present study is the diagnostic contribution of antibodies against deamidated gliadin peptides (anti-DGP). In our cohort, IgG anti-DGP antibodies were positive in 48.97% ($n = 24$) of patients with celiac disease, representing a slightly higher positivity rate than that observed for IgG anti-tTG (40.81%), while no healthy control tested positive (Figures 3 and 4). These findings confirm the excellent specificity of anti-DGP antibodies in our study population and support their usefulness as complementary biomarkers to IgA anti-tTG testing.

These results are consistent with previous reports showing that IgG anti-DGP antibodies exhibit a diagnostic sensitivity ranging from 74% to 88% and a specificity generally exceeding 95%. Several studies have also demonstrated that anti-DGP antibodies can be detected in a subset of patients with histologically confirmed celiac disease despite negative conventional serological markers, highlighting their value in serologically atypical forms of the disease. Furthermore, a recent study evaluating a combined screening strategy based on IgA anti-tTG and IgG anti-DGP reported a sensitivity of 84.3% and a specificity of 90.1%, confirming that an integrated serological approach improves diagnostic performance without substantially compromising specificity [11,13–15].

Our findings further support the observations reported by Rashtak et al., who demonstrated that the combined assessment of anti-tTG and anti-DGP antibodies optimizes the diagnostic performance of celiac disease screening. This combined strategy not only confirms positive IgA anti-tTG results but also improves the overall detection rate by identifying patients who fail to develop anti-tTG antibodies or who present with selective IgA deficiency [16]. In our study, the higher positivity rate observed for IgG anti-DGP compared with IgG anti-tTG suggests that anti-DGP antibodies provide

additional diagnostic information and may represent the most informative IgG biomarker when complementary serological testing is required.

The diagnostic value of anti-DGP antibodies appears to be particularly relevant in specific patient subgroups. Current international guidelines and several recent reviews emphasize their usefulness in young children, especially those younger than two years of age, in whom the IgA-mediated humoral immune response may still be immature, as well as in patients with selective IgA deficiency, for whom IgG-based serological tests play a central role in the diagnostic algorithm. Although our study was not designed to perform stratified analyses according to age or IgA status, the high proportion of pediatric patients with celiac disease (65%) may, at least partially, explain the relatively high frequency of IgG anti-DGP positivity observed in our cohort. This finding is consistent with current recommendations advocating the use of anti-DGP antibodies in these specific clinical settings and further supports the inclusion of IgA anti-tTG and IgG anti-DGP within an expanded serological panel to improve diagnostic yield, particularly in pediatric populations and in patients with a high clinical suspicion despite negative conventional serology [9,10,17].

The superior diagnostic performance observed for anti-DGP antibodies may be explained by the immunogenic properties of deamidated gliadin peptides, particularly the PLQPEQFPF and PEQLPQFEE epitopes, which exhibit high affinity for HLA-DQ2 and HLA-DQ8 molecules and elicit a strong antigen-specific humoral immune response in genetically predisposed individuals [18]. This mechanism may account for the ability of anti-DGP antibodies to identify certain patients in whom anti-tTG antibodies remain undetectable or are expressed at very low levels.

Taken together, these findings support the implementation of a combined serological strategy based on the association of IgA anti-tTG and IgG anti-DGP, rather than reliance on a single biomarker. Such an approach may improve the sensitivity of celiac disease screening, particularly in patients with atypical presentations, selective IgA deficiency, or persistent clinical suspicion despite initially negative serological findings, while maintaining excellent diagnostic specificity.

The present study also provides additional evidence supporting the diagnostic relevance of anti-tissue transglutaminase (anti-tTG) and anti-deamidated gliadin peptide (anti-DGP) antibodies in the serological diagnosis of celiac disease. In our cohort, the absence of antibody positivity among healthy controls suggests excellent diagnostic specificity for both autoantibodies. However, these findings should be interpreted cautiously given the relatively small sample size and the single-center design of the study, which preclude a precise estimation of the diagnostic accuracy of the different serological markers.

Among patients with celiac disease, positivity for at least one IgA autoantibody was observed in 87.75% ($n = 43$) of cases, confirming that the humoral immune response directed against tissue transglutaminase and deamidated gliadin peptides is present in the majority of affected individuals. Isolated IgA anti-tTG positivity was the most frequent serological profile (40.81%; $n = 20$), further supporting its role as the first-line serological marker for celiac disease. Nevertheless, isolated IgA anti-DGP positivity, observed in 28.57% ($n = 14$) of patients, indicates that these antibodies provide complementary diagnostic information and may identify patients in whom anti-tTG antibodies are not detectable (Figure 5).

The coexistence of IgA anti-tTG and IgA anti-DGP positivity was observed in 18.36% ($n = 9$) of patients (Figure 5), representing another noteworthy finding. Although our study did not include quantitative antibody measurements or systematic correlations with histopathological findings, this dual positivity may reflect a more pronounced humoral immune response. Conversely, 12.24% ($n = 6$) of patients were negative for both IgA markers (Figure 5). This observation highlights that, despite its excellent diagnostic performance, serology alone cannot definitively exclude celiac disease. Several factors may account for seronegative profiles, including early-stage disease, selective IgA deficiency, or serologically silent forms of celiac disease.

Regarding IgG autoantibodies, at least one IgG marker was positive in 61.22% ($n = 30$) of patients (Figure 6), a lower frequency than that observed for IgA antibodies (87.75%) (Figure 5), which is consistent with the predominant role of IgA-mediated immune responses in immunocompetent individuals. Nevertheless, IgG antibodies remain diagnostically valuable in specific clinical settings, particularly in patients with selective IgA deficiency or in those with persistent clinical suspicion despite negative IgA serology. In our cohort, isolated IgG anti-DGP positivity (20.40%; $n = 10$) was more frequent than isolated IgG anti-tTG positivity (12.24%; $n = 6$), suggesting that anti-DGP antibodies may provide additional diagnostic value in selected serological profiles.

The overall analysis of serological profiles highlights the complementary nature of the different biomarkers. The presence of isolated positivity for each antibody suggests that a diagnostic strategy relying on a single serological marker may fail to identify a subset of patients with celiac disease. This finding is consistent with several studies demonstrating that the combined assessment of anti-tTG and anti-DGP antibodies improves the detection of celiac disease, particularly in atypical or oligosymptomatic presentations and in patients with an intermediate pre-test probability. However, the literature also emphasizes that the routine use of an expanded serological panel should be carefully considered, as the addition of anti-DGP antibodies may reduce overall specificity when positivity

thresholds are not appropriately optimized or when testing is performed in populations with a low pre-test probability of disease. Furthermore, isolated IgG anti-DGP positivity is not invariably associated with histologically confirmed celiac disease, highlighting the need to interpret serological findings in conjunction with clinical, laboratory, and histopathological data [8,10,14,19].

Overall, our findings are consistent with current international recommendations, which place IgA anti-tTG testing, together with the measurement of total serum IgA, at the center of the diagnostic algorithm for celiac disease. IgG-based serological tests, particularly anti-DGP antibodies, are primarily recommended for patients with selective IgA deficiency or when a strong clinical suspicion persists despite negative IgA serology. In addition, the increasing adoption of biopsy-sparing diagnostic strategies in carefully selected patients with markedly elevated IgA anti-tTG titers further underscores the growing role of serology in the diagnosis of celiac disease. However, our study was not designed to evaluate this approach because quantitative measurements of antibody titers were not available [8,9,10,13,14].

Our findings are of particular relevance in the Moroccan context. Regional data regarding the diagnostic performance of serological biomarkers for celiac disease remain limited, while access to upper gastrointestinal endoscopy, expert histopathological evaluation, and specialized diagnostic facilities varies considerably across healthcare settings. Under these circumstances, a stepwise diagnostic strategy appears especially appropriate. Measurement of IgA anti-tTG, together with total serum IgA, should remain the first-line investigation, whereas anti-DGP antibodies, particularly those of the IgG isotype, may be used selectively in patients with IgA deficiency, discordant serological findings, or persistent clinical suspicion despite an initially negative serological evaluation. Such an approach may improve case detection while taking into account the organizational and economic constraints of resource-limited healthcare systems.

This study has several limitations. Its retrospective design, single-center setting, and relatively small sample size limit the generalizability of the findings. Furthermore, the use of a semi-quantitative immunodot assay precluded the evaluation of diagnostic performance across different positivity thresholds and did not allow calculation of predictive values, likelihood ratios, or receiver operating characteristic (ROC) curves. In addition, the absence of systematic correlation with histopathological findings prevented assessment of the relationship between serological profiles and the severity of intestinal mucosal lesions.

Despite these limitations, this study provides original data in a field where evidence from North African populations remains scarce. Our findings demonstrate the complementary diagnostic value of anti-tTG and anti-DGP antibodies and

emphasize the importance of interpreting serological markers within the broader clinical context and in accordance with current international recommendations. Future prospective multicenter studies involving larger patient cohorts, quantitative antibody assays, systematic histopathological correlation, and cost-effectiveness analyses are warranted to better define the respective roles of these biomarkers in the diagnosis of celiac disease.

CONCLUSION

Our findings highlight the value of a multi-marker serological approach for the diagnosis of celiac disease by demonstrating the complementary roles of anti-tTG and anti-DGP antibodies. While IgA anti-tTG remains the cornerstone of current international diagnostic recommendations, the targeted incorporation of anti-DGP antibodies may enhance diagnostic yield, particularly in clinical settings where the performance of conventional serological biomarkers is suboptimal. By providing original data from a Moroccan population, this study contributes to expanding current knowledge on the diagnostic performance of serological biomarkers for celiac disease in North African countries. It also underscores the importance of adapting diagnostic strategies to resource-limited healthcare settings, where optimizing non-invasive diagnostic tools represents a major clinical and economic challenge. Large prospective multicenter studies incorporating quantitative antibody assays, histopathological correlation, and cost-effectiveness analyses are warranted to better define the role of anti-DGP antibodies within international diagnostic guidelines and to identify the patient populations most likely to benefit from a combined serological strategy.

Acknowledgements

Conflict of Interest

We declare that there are no conflicts of interest to disclose.

Authors Contribution

The authors of this article have made significant contributions to the design, data collection, analysis, and manuscript writing. Their individual contributions are as follows:

Pr. Nabil Gaougaou: Supervision, Conceptualization, Validation, Revision and Editing.

Dr. Aazzane Oussama: Writing - original version, Conceptualization, Methodology, Data collection.

Dr. Bazhar Hasnaa: Formal analysis, Visualization.

Pr. Fellah Hassan: Investigation, Supervision, Conceptualization, Methodology, Validation, Revision and Editing.

Availability of Data

The data used in this research is available upon request from the authors (Dr. Oussama Aazzane, and Pr. Hassan Fellah).

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