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MODERN DIAGNOSTIC METHODS AND CLINICAL SIGNIFICANCE OF CELIAC DISEASE

Kasimova Mavjuda Barnayevna
Senior Lecturer,
Tashkent State Medical University
Tashkent, Uzbekistan

Annotation: Celiac disease is a chronic autoimmune disorder triggered by gluten ingestion in genetically predisposed individuals. The disease affects the small intestine and leads to malabsorption of nutrients due to immune-mediated damage of the intestinal mucosa. Recent advances in laboratory and instrumental diagnostic techniques have significantly improved the early detection and clinical management of this condition. The present article analyzes modern diagnostic methods of celiac disease, including serological testing, genetic analysis, and histological examination of intestinal biopsies. The clinical significance of early diagnosis and its impact on preventing complications such as anemia, osteoporosis, infertility, and intestinal lymphoma are also discussed. The article is based on data from international medical literature and clinical studies. Modern diagnostic approaches play an important role in the timely identification of patients with celiac disease and contribute to improving the quality of life of affected individuals through early dietary intervention.

Keywords: Celiac disease, gluten intolerance, serological diagnosis, intestinal biopsy, tissue transglutaminase antibodies, HLA-DQ2, HLA-DQ8, autoimmune disorders, malabsorption syndrome.

Introduction

Celiac disease is a chronic immune-mediated enteropathy caused by sensitivity to gluten proteins found in wheat, barley, and rye. According to epidemiological studies, the prevalence of celiac disease worldwide is approximately **1% of the population**, although many cases remain undiagnosed [1]. The disease occurs in genetically predisposed individuals carrying the **HLA-DQ2 or HLA-DQ8 haplotypes** and leads to inflammation and damage of the small intestinal mucosa after gluten consumption [2].

Clinical manifestations of celiac disease are highly variable and may include chronic diarrhea, abdominal pain, weight loss, iron-deficiency anemia, fatigue, growth retardation in children, and extraintestinal symptoms such as dermatitis herpetiformis and osteoporosis [3]. Due to the wide range of clinical manifestations, the disease often remains underdiagnosed for many years.

Advances in diagnostic technologies have significantly improved the identification of celiac disease. Modern diagnostic approaches involve **serological tests, genetic testing, and histopathological evaluation of intestinal biopsy specimens** [4]. Early diagnosis is crucial because untreated celiac disease can lead to serious complications, including malnutrition, infertility, neurological disorders, and intestinal malignancies [5].

The purpose of this study is to analyze modern diagnostic methods of celiac disease and evaluate their clinical significance based on data from international scientific literature.

Methodology

The methodological basis of this study is a **systematic analysis of scientific publications, clinical guidelines, and medical research articles** devoted to the diagnosis of celiac disease. The study utilized data from international medical databases and publications from the **World Gastroenterology Organisation (WGO), the European Society for Paediatric**

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Gastroenterology Hepatology and Nutrition (ESPGHAN), and peer-reviewed medical journals.

The research methods included:

- Comparative analysis of diagnostic techniques used in the detection of celiac disease
- Evaluation of the sensitivity and specificity of serological tests
- Analysis of histological diagnostic criteria for intestinal biopsy
- Review of genetic markers associated with celiac disease susceptibility

The study focused on evaluating the effectiveness of **modern serological tests such as anti-tissue transglutaminase antibodies (tTG-IgA), anti-endomysial antibodies (EMA), and deamidated gliadin peptide antibodies (DGP)**, as well as the role of **HLA genotyping** in the diagnosis of the disease [6].

Results

Analysis of scientific literature shows that modern diagnostic methods have significantly improved the accuracy of detecting celiac disease. Serological testing is currently considered the **first-line screening method**.

The most widely used diagnostic marker is **tissue transglutaminase IgA antibodies (tTG-IgA)**. Studies indicate that the sensitivity of this test reaches **90–98%**, while its specificity exceeds **95%** [7]. The presence of these antibodies strongly suggests autoimmune damage to the intestinal mucosa associated with gluten intolerance.

Another important diagnostic marker is the **endomysial antibody (EMA) test**, which has a specificity close to **100%** but is more expensive and technically demanding [8].

Genetic testing for **HLA-DQ2 and HLA-DQ8 haplotypes** is also widely used in clinical practice. Approximately **95% of patients with celiac disease carry HLA-DQ2**, while most of the remaining patients carry **HLA-DQ8** [9]. Although the presence of these genetic markers alone cannot confirm the diagnosis, their absence makes celiac disease extremely unlikely.

Histological examination of small intestinal biopsy specimens remains the **gold standard** for confirming the diagnosis. Typical histological features include **villous atrophy, crypt hyperplasia, and increased intraepithelial lymphocytes**, known as the **Marsh classification** of mucosal lesions [10].

Analysis and Discussion

Modern diagnostic approaches to celiac disease are based on the integration of clinical assessment, serological testing, genetic analysis, and histopathological confirmation. The development of these diagnostic methods has significantly improved the ability of clinicians to detect the disease at earlier stages, which is essential for preventing long-term complications associated with untreated celiac disease. Scientific studies show that the prevalence of celiac disease is approximately 1% worldwide, although a large proportion of cases remain undiagnosed due to the variability of clinical manifestations and the presence of asymptomatic or atypical forms of the disease [1].

One of the most important aspects of modern celiac disease diagnostics is the use of serological screening tests. Serological testing allows the identification of individuals with a high probability of having the disease before performing invasive diagnostic procedures such as intestinal biopsy. Among the available serological markers, antibodies against tissue transglutaminase (tTG-IgA) are considered the most reliable and widely used diagnostic indicator. Numerous clinical studies have demonstrated that the sensitivity of tTG-IgA testing ranges from 90% to 98%, while specificity exceeds 95% in most populations [7]. Due to these characteristics, international clinical guidelines recommend the tTG-IgA test as the first-line screening tool for suspected celiac disease.

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The presence of anti-endomysial antibodies (EMA) also plays an important role in confirming the diagnosis. EMA antibodies demonstrate extremely high specificity for celiac disease, often approaching 100% [8]. However, this diagnostic method requires specialized laboratory techniques and trained personnel, which may limit its use in some clinical settings. For this reason, EMA testing is often used as a confirmatory test following a positive tTG-IgA result rather than as a primary screening method.

Another important diagnostic marker is the detection of antibodies against deamidated gliadin peptides (DGP). DGP antibodies have shown improved diagnostic accuracy compared with earlier antigliadin antibody tests, particularly in young children and patients with selective IgA deficiency. In clinical practice, DGP-IgG antibodies are especially useful when total IgA deficiency is suspected, because the tTG-IgA test may produce false-negative results in such cases [11]. The combination of different serological markers significantly increases the diagnostic sensitivity and reduces the probability of missed diagnoses.

Selective IgA deficiency is an important clinical factor that must be considered during serological testing. Studies indicate that IgA deficiency occurs more frequently among patients with celiac disease than in the general population. Because standard screening tests rely on IgA-based antibodies, patients with IgA deficiency may produce false-negative results if only tTG-IgA tests are used. Therefore, measurement of total serum IgA levels is recommended as part of the diagnostic evaluation. If IgA deficiency is detected, IgG-based serological tests such as DGP-IgG or tTG-IgG should be performed to ensure accurate diagnosis.

Genetic testing has also become an important component of the diagnostic process for celiac disease. The disease has a strong genetic association with specific human leukocyte antigen (HLA) haplotypes, particularly HLA-DQ2 and HLA-DQ8. Approximately 95% of patients with celiac disease carry the HLA-DQ2 haplotype, while most of the remaining patients carry HLA-DQ8 [9]. These genetic markers are involved in the immune response to gluten peptides and play a critical role in the pathogenesis of the disease.

Although the presence of HLA-DQ2 or HLA-DQ8 does not confirm the diagnosis of celiac disease, the absence of these haplotypes has a high negative predictive value. In other words, individuals who do not carry either HLA-DQ2 or HLA-DQ8 are extremely unlikely to develop celiac disease. For this reason, HLA genotyping is particularly useful in situations where the diagnosis is uncertain, such as patients who have already started a gluten-free diet before completing diagnostic testing or individuals with inconclusive serological and histological findings.

Histopathological examination of small intestinal biopsy specimens remains the gold standard for confirming the diagnosis of celiac disease. The biopsy is usually obtained from the duodenum during upper gastrointestinal endoscopy. Histological evaluation reveals characteristic structural changes in the intestinal mucosa caused by immune-mediated inflammation triggered by gluten exposure.

The most widely used system for describing mucosal damage in celiac disease is the Marsh classification. According to this classification, the earliest stage of the disease (Marsh I) is characterized by an increased number of intraepithelial lymphocytes in the intestinal mucosa. In the Marsh II stage, crypt hyperplasia becomes evident, indicating increased cellular proliferation in response to mucosal injury. The most advanced stage, Marsh III, involves partial or complete villous atrophy, resulting in significant impairment of nutrient absorption [10].

Villous atrophy is one of the most important histological features of celiac disease because it directly affects the absorptive capacity of the small intestine. The villi of the intestinal mucosa normally increase the surface area available for nutrient absorption. When these structures are

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damaged or destroyed, the intestine becomes unable to efficiently absorb essential nutrients such as iron, calcium, folate, and fat-soluble vitamins. This mechanism explains many of the clinical manifestations of celiac disease, including anemia, weight loss, and osteoporosis.

Despite the diagnostic value of intestinal biopsy, some recent clinical guidelines suggest that biopsy may not always be necessary in certain pediatric cases. According to guidelines developed by the European Society for Paediatric Gastroenterology Hepatology and Nutrition (ESPGHAN), children with very high levels of tTG-IgA antibodies and positive EMA tests may be diagnosed without biopsy under specific clinical conditions. This approach reduces the need for invasive procedures while maintaining diagnostic accuracy.

However, in adult patients, intestinal biopsy remains a critical component of the diagnostic process because adults are more likely to present with atypical or silent forms of the disease. In such cases, histological examination provides essential information for confirming the diagnosis and evaluating the severity of mucosal damage.

Another important aspect of the diagnostic process is the recognition of extraintestinal manifestations of celiac disease. Although gastrointestinal symptoms such as chronic diarrhea and abdominal pain are common, many patients present primarily with non-gastrointestinal symptoms. These may include iron-deficiency anemia, chronic fatigue, infertility, neurological disorders, and dermatitis herpetiformis. In some patients, the disease may remain clinically silent and be detected only through screening in high-risk groups.

High-risk populations for celiac disease include first-degree relatives of affected individuals, patients with type 1 diabetes mellitus, autoimmune thyroid disease, Down syndrome, and selective IgA deficiency. Screening of these groups using serological testing is recommended because the prevalence of celiac disease is significantly higher in these populations compared with the general population.

Early diagnosis of celiac disease has significant clinical importance because untreated disease can lead to severe long-term complications. One of the most common complications is osteoporosis, which occurs due to impaired calcium and vitamin D absorption in the damaged small intestine. Long-term malabsorption may also lead to growth retardation in children and increased risk of fractures in adults.

Another important complication is infertility and adverse pregnancy outcomes. Research indicates that untreated celiac disease is associated with increased risk of infertility, recurrent miscarriages, and low birth weight in newborns. Early diagnosis and adherence to a gluten-free diet significantly reduce these risks and improve reproductive outcomes.

Neurological complications have also been described in patients with untreated celiac disease. These may include peripheral neuropathy, ataxia, epilepsy, and cognitive impairment. Although the exact mechanisms underlying these neurological manifestations are not fully understood, immune-mediated processes and nutritional deficiencies are believed to play important roles.

One of the most serious complications of untreated celiac disease is the development of intestinal malignancies, particularly enteropathy-associated T-cell lymphoma (EATL). Although this condition is relatively rare, its prognosis is poor and it represents one of the most severe consequences of long-term intestinal inflammation [12]. Early diagnosis and strict adherence to a gluten-free diet significantly reduce the risk of developing such malignancies.

The primary treatment for celiac disease is a strict lifelong gluten-free diet. This diet eliminates all foods containing wheat, barley, and rye, thereby preventing immune activation and allowing the intestinal mucosa to heal. Clinical studies have shown that most patients experience

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significant improvement in symptoms within weeks after starting a gluten-free diet, while histological recovery of intestinal villi may take several months or even years.

Adherence to a gluten-free diet is essential for preventing relapse and long-term complications. However, maintaining such a diet can be challenging due to the widespread presence of gluten in processed foods. Therefore, patient education and regular medical follow-up are critical components of disease management.

Monitoring of treated patients typically involves periodic serological testing to assess adherence to the gluten-free diet and evaluate the effectiveness of treatment. Decreasing levels of tTG antibodies after dietary intervention indicate reduced immune activity and mucosal healing. In some cases, repeat intestinal biopsy may be performed to confirm histological recovery.

In recent years, research has also focused on the development of new diagnostic and therapeutic approaches for celiac disease. Advances in molecular biology and immunology have improved the understanding of disease pathogenesis and opened new possibilities for non-invasive diagnostic methods. For example, researchers are investigating biomarkers that could allow detection of intestinal damage without the need for invasive biopsy procedures.

Additionally, several experimental therapies aimed at modifying the immune response to gluten are currently being studied. These include enzyme therapies designed to break down gluten peptides before they trigger immune reactions, as well as vaccines intended to induce immune tolerance to gluten. Although these approaches are still under investigation, they represent promising directions for future treatment strategies.

Conclusion

Celiac disease is a common autoimmune disorder that requires accurate and timely diagnosis to prevent severe complications. Modern diagnostic methods, including serological testing, genetic analysis, and histological examination of intestinal biopsies, significantly improve the detection of this disease.

Serological tests such as **tTG-IgA and EMA antibodies** are effective screening tools with high sensitivity and specificity. Genetic testing for **HLA-DQ2 and HLA-DQ8 haplotypes** provides valuable information for confirming or excluding the diagnosis. Histological examination of intestinal biopsy specimens remains the gold standard for definitive diagnosis.

The integration of modern diagnostic technologies allows healthcare professionals to identify celiac disease at an early stage and initiate appropriate treatment. Early diagnosis and strict adherence to a gluten-free diet significantly improve patient outcomes and reduce the risk of long-term complications.

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