RECENT UPDATE AND FUTURISTIC TRENDS IN DIAGNOSIS AND TREATMENT OF "CELIAC **DISEASE**"

Abstract

Foods containing gluten can cause Ms. Shraddha Patidar disease, which is long-term celiac a immunological and digestive illness that harms and affects the small intestine. Our body is unable to receive all the nutrients which it needs because of this disease. Gluten is a protein found in grains such as wheat, barley, rye, and others. Gluten makes dough stretchy and gives bread its chewy texture. The small intestine and villi, tiny finger-like projections seen on the small intestine wall, are damaged when the patient with celiac disease consumes food containing gluten because their body overreacts to the gluten protein. The small intestine cannot absorb enough nutrients from food when these villi are destroyed. In the end, this causes starvation, miscarriage, infertility, bone density loss, and neurological disorders. Researchers still don't have a firm understanding of the cause of celiac disease. Due to its inherited nature, celiac disease may pass on to certain genes. Any traumatic emotional experience or a severe medical incident can set it off. To help identify celiac disease, a tissue test for transglutaminase IgA (tTg-IgA) is employed. In this autoimmune illness, the immune system misinterprets the protein gluten as an outside invader.

Keywords: Celiac disease, Gluten, tissue transglutaminase IgA (tTg-IgA), Gluten free diet.

Authors

Institute of Pharmaceutical Sciences Sage University Indore, India.

Dr. Souravh Bais

Institute of Pharmaceutical Sciences Sage University Indore, India.

I. INTRODUCTION

Foods containing gluten triggers celiac disease which is considered as a chronic digestive and immune disorder in this it affects and damages the small intestine. Gluten containing food triggers the celiac disease. It causes long lasting digestive problems and insufficient amount of nutrients are absorbed from the food. Other names for celiac disease include celiac sprue, glutensensitive enteropathy, and non-tropical sprue. A protein named gluten is present in barely, wheat, rye and other grains. Gluten gives elasticity to the dough and gives bread its chewy texture.

When a person with celiac disease consumes food containing gluten, their body overreacts to the gluten protein, causing damage to the small intestine and villi, microscopic projections that resemble fingers and are visible on the small intestine wall. When these villi are lost, the small intestine is unable to absorb enough nutrients from food. In the end, this results in neurological diseases, infertility, bone density loss, miscarriage, and famine. When the patient is on gluten free diet for a year and isn't getting better than it is called refractory or non-responsive celiac disease. Most of the times the patient never know they have celiac disease due to slow damage of small intestine and varied symptoms leads to several years to diagnose the disease. Even though the patient is on a gluten-free diet and exhibits the same symptoms, the body does not display intestinal damage. [1-2]

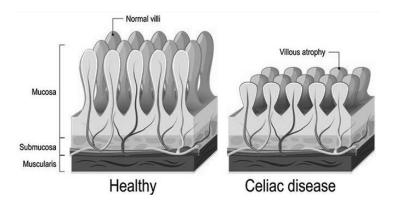


Figure 1: Figure showing the difference in shape of villi in celiac disease

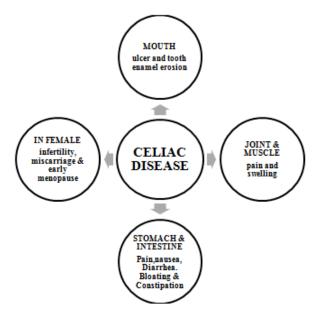


Figure 2: Figure Showing the Complications Related to Celiac Disease in Other Organs of Body

II. CELIAC DISEASE SYMPTOMS

Food allergy can't be concluded as celiac disease as the symptoms are varied. If the patient is allergic to wheat and consumes wheat then they may have symptoms like itchy or watery eyes or hard time breathing.

- 1. Symptoms of Celiac Disease in Adults: If a celiac disease patient accidentally consumes glutencontaining food, they may have symptoms such as:
 - Anemia
 - Abdominaldiscomfort
 - Boneorjointpain
 - Bloatingor feelingfullness
 - Constipation
 - Diarrhea
 - Gas
 - Heartburn
 - Itchy,blisteryrash(dermatitisherpetiformis, according to doctors)
 - Headachesorexhaustion
 - Mouthulcers
 - Nausea
 - Nervoussysteminjury, such as numb or tingling hands or feet, balance issues, or changes in consciousness
 - Poopthatispale, stinks, or floats (steatorrhea)
 - Weight reduction

Celiac disease can also result in decreased spleen function (hyposplenism) and a loss of bone density.

- **2. Children's Celiac Disease Symptoms:** Intestinal problems are more likely in children with celiac disease, including:
 - Bellyswellingorbloating
 - Diarrhea
 - Pale,foul-smellingpoop
 - Weightloss
 - Constipation
 - Upsetstomachorvomiting

If celiac disease prevents a child's body from absorbing the nutrients they require, they may experience the following symptoms:

- Anemia
- Damaged tooth enamel
- Infant failure to thrive
- Slow growth and short stature
- Delayed puberty
- Crankiness or mood changes
- Neurological issues such as learning impairments and attention deficit hyperactivity disorder (ADHD)

These symptoms are not experienced by everyone who has celiac disease. Some people do not notice any abnormalities, making diagnosis difficult.

Dermatitis herpetiformis (celiac rash)

Out of 4 people 1 with celiac disease gets blisters and itchy rashes. Adults and women are more prone to celiac rashes and it mostly happens in these body parts.

- Knees
- Scalp
- Elbows
- Buttocks
- Lowerback[1-3]
- **3.** Celiac Disease Causes and Risk Factors: There is no definite cause of celiac disease known yet. Celiac disease is inheriting in nature and may continue to certain genes. Any emotional trauma or stressful medical events can trigger it. A transglutaminase IgA (tTg-IgA) tissue test is used to help diagnose celiac disease. If the family member is diagnose to celiac disease, and then there is 1 in 10 chance of getting celiac disease.

Caucasians are more prone to celiac disease and people with other diseases, including:

- Addison's disease
- Down syndrome
- Hashimoto's thyroiditis
- Type 1 diabetes
- Chronic pancreatitis
- Ig A nephropathy
- Idiopathic dilated cardiomyopathy
- Lupus
- Rheumatoid arthritis
- Turner syndromei(in which a female lacks an Xichromosome)
- Multiple sclerosis (MS)
- Autoimmune hepatitis Sjogren's syndrome
- Psoriasis
- Williams's syndrome
- Primary biliary cirrhosis
- Intestinal lymphoma
- Intestinal cancer
- Lactose intolerance
- Irritable bowel syndrome (IBS)
- Scleroderma

III. CELIAC DISEASE COMPLICATIONS

If not treated the celiac disease can be threatening to life. Complications may include:

- Malnutrition
- Lactose intolerance
- Infertility and miscarriage
- Tooth enamel damage
- pancreatic disease
- Cancer, especially intestinal lymphoma and small intestine cancer
- Nervous system issues such as seizures or pain and numbness in your hands and feet (peripheral neuropathy)
- Bone weakness[3-5]
- **1.** Celiac Disease Tests and Diagnosis: To diagnose celiac disease, blood tests and other procedures are performed:
 - Metabolic panels assess the function of the liver and kidneys.
 - Iron and ferritin tests are used to detect iron deficiency.
 - Swallowing a tiny camera can reveal digestive system issues.
 - Serology tests search for specific antibodies.
 - Blood tests examine different aspects of your immune system.

- Intestinal fatty acid binding protein assays detect intestinal damage.
- A complete blood count detects anemia (low red blood cell count).
- C-reactive protein testing reveal whether or not there is inflammation.
- Vitamin D, B12, and folate tests are used to detect vitamin deficits.
- Imaging scans detect changes in the intestine, such as wall thickening or blood vessel alterations.
- To rule out celiac disease, genetic testing searches for human leukocyte antigens.

If blood testing and other tests reveal that you have celiac disease, an endoscopy is required for confirmation. Endoscopy is a procedure in which a small piece of tissue is removed to confirm intestinal injury. [6]

- 2. Causes: The immune system is triggered by gluten to damage villi. Most of the nutrients are absorbed from the food and sent to bloodstream with the help of Villi (VIL-eye) which are finger like projections lining the small intestine. If the Villi gets damaged it does not absorb the vitamins and minerals which a child needs to grow. There is no definite cause of celiac disease known yet. Celiac disease is inheriting in nature and may continue to certain genes. Caucasians are more prone to celiac disease and people with other diseases, including Down syndrome, Williams's syndrome, type 1 diabetes, and autoimmune thyroid disorders. [7-8]
- **3.** Celiac Disease Diagnosis: A blood test confirms the presence of celiac disease, and antibodies are tested for gluten and other proteins on the villi. Antibodies are chemicals that operate against undesirable compounds in the body by blocking or killing them. These are created by the immunological system.

A biopsy is performed to determine the amount of antibodies in the blood. A long thin tube (Endoscope) is passed via the mouth and stomach into the small intestine during this surgery, and a little tissue sample is obtained for testing.

A blood test to screen for antibodies to gluten and other proteins in the gut lining is commonly used to diagnose celiac disease. Antibodies are proteins produced by the immune system that recognize and eliminate pathogens and other dangers. They typically remain in our bodies in case we need to tackle the same virus or disease again. If the blood test reveals high levels of gluten antibodies, the doctor will most likely perform a sample of the small intestine for testing. In pediatrics, the patient is sedated by general anesthesia and put to sleep for the biopsy[8-13].

IV. DIAGNOSIS - TISSUE TRANSGLUTAMINASE IGA (TTG-IGA)

The tissue transglutaminase (tTg-IgA) test is used to diagnose celiac disease. Celiac disease is an autoimmune condition in which the body's immune system views gluten as a foreign invader.

In the intestine, antibodies assault an enzyme called tissue transglutaminase (tTG). Antibodies (immunoglobulins) bind to pathogens and kill them.

- 1. tTG-IgA Tests: If a patient has celiac disease and exhibits symptoms such as vomiting, diarrhea, constipation, gut pain, poor growth, or rashes, a tTG-IgA test may be ordered. The test is also performed on patients who have type 1 diabetes, thyroid disease, or a family member who has celiac disease.
- 2. Prepare for a tTG-IgA Test: For the accurate results of the blood test, the patient should be on normal diet or the gluten containing diet until the test is completely performed.

V. IMMUNOGLOBULIN TEST

The immunoglobulin test measures the amounts of different types of antibodies in the blood. The immune system protects the body from germs, viruses, and allergies. Different antibodies are produced by the body to protect against various threats. In the instance of autoimmune disease, the body produces antibodies against itself or healthy organs and tissues, mistaking them for foreign invaders.

The Types of Antibodies are:

- **1. Immunoglobulin A (IgA):** This protein is found in the linings of the respiratory and digestive tracts, as well as saliva (spit), tears, and breast milk.
- **2. Immunoglobulin G (IgG):** This is the most commonly encountered antibody. It is found in blood and other bodily fluids and provides protection against bacterial and viral diseases. After an infection or immunization, IgG can take some time to develop.
- **3.** Immunoglobulin M (IgM): Found primarily in blood and lymph fluid, this is the first antibody produced by the body when it encounters a new infection.
- **4. Immunoglobulin E (IgE):** Found at low levels in the blood. When the body overreacts to allergens or is fighting a parasite infection, there may be increased levels.
- **5. Immunoglobulin D** (**IgD**): This antibody is the least understood, with just trace levels seen in the blood.[14-18]

Table 1: Commonly Used Diagnostic Tests for Celiac Disease

| Test | Advantages | Disadvantages |
|-------------------------|-----------------------------|------------------------------------|
| Tissue transglutaminase | Most reliable noninvasive | Falsely negative with IgA |
| tTG IgA antibodies | test first level screening | deficiency (3% of patients with |
| | test High sensitivity and | celiac disease) |
| | specificity | May be negative if on low – gluten |
| | | diet |
| Tissue transglutaminase | Useful in patients with IgA | Widely variable sensitivity and |
| tTG IgG antibodies | deficiency | specificity |

| IgA antiendomysial | May be useful in patients | Sensitivity for celiac disease less |
|----------------------|---|-------------------------------------|
| antibodies | with borderline results for | than IgA anti- transglutaminase |
| | tTG antibodies | antibody test |
| IgGdeamidatedgliadin | Useful in patients with IgA | Not as sensitive or specific as tTG |
| peptide antibodies | deficiency and in young | IgA antibodies |
| | children | |
| HLA-DQ2 or HLA-DQ8 | High negative predictive value for celiac disease | Test is complex and expensive |
| Small bowel biopsy | Reliable test considered | Requires endoscopy and biopsy |
| | gold standard | very expensive |
| | Reflects response to | |
| | treatment | |

6. Why Are Immunoglobulin Tests Done?

Immunoglobulin tests are used to determine whether a person is infected or at risk of infection. The immunoglobulin test is used to diagnose immunodeficiency. Immunodeficiencies are possible in children who are exposed to uncommon illnesses. This test can detect allergies or autoimmune illnesses such as arthritis, lupus, and celiac disease.

VI. HOW IS CELIAC DISEASE TREATED?

There is currently no cure or treatment for celiac disease. Many studies are being conducted on new treatments. For the time being, a gluten-free diet can help mend the intestinal lining or villi and alleviate [19-25]

VII.DIETARY CHANGES

Professionals advise on which diet to follow and which foods to avoid. These minor improvements will alleviate symptoms and have a significant impact on daily living. Dietitians can advise you on which diet to follow.

Gluten-free foods should not contain rye, barley, wheat, or other similar grains. In most countries, all food labels must include any of the top eight food allergens, including gluten-containing cereals. Many wheat-free goods may contain gluten-containing grains such as rye or barley.

Before purchasing, carefully read the labels. Many foods and beverages are listed on the celiac disease foundation's website.

1. Gluten-Free Foods Include

- Fruits
- Vegetables
- Meat and poultry

- Fish and other seafood
- Dairy
- Beans and nuts

2. Some Gluten-Free Starches and Grains Include:

- Rice
- Corn or maize
- Soy
- Potato
- Tapioca
- Beans
- Sorghum
- Ouinoa
- Millet
- Amaranth
- Flax
- Chia
- Nut flours
- Common things such as pharmaceuticals and toothpaste might contain gluten, so read the label carefully.[23-28]

VIII. CONCLUSION

The extensive literature review indicates that gluten containing foods cause celiac disease, which is a chronic digestive and immunological illness that affects and damages the small intestine. This disease causes severe digestive issues and prevents our bodies from receiving all of the nutrients they require. Gluten is a protein found in wheat, barley, rye, and other cereals. Gluten gives dough flexibility and gives bread its chewy texture. Gluten gives the dough flexibility and gives bread its chewy texture. When a celiac disease patient consumes gluten-containing foods, their body over re-acts to the gluten protein, causing damage to the small intestine and villi, which are little finger like projections on the small intestinal wall. Gluten is a protein found in grains such as barely, wheat, rye, and others. Gluten gives the dough flexibility and gives bread its chewy texture. When a celiac disease patient consumes gluten-containing foods, their body over reacts to the glut en protein, causing damage to the small intestine and villi, which are little finger-like projections on the small intestinal wall. When these villi are destroyed, the small intestine is unable to absorb enough nutrients from food. This eventually leads to starvation, miscarriage, infertility, bone density loss, and neurological problems.

A biopsy is performed to determine the amount of antibodies in the blood. A long thin tube (Endoscope) is passed via the mouth and stomach into the small intestine during this surgery, and a little tissue sample is obtained for testing. The tissue transglutaminase (tTg-IgA) test is used to diagnose celiac disease. Celiac disease is an autoimmune condition in which the

body's immune system views gluten as a foreign invader. In the intestine, antibodies assault an enzyme called tissue transglutaminase (tTG). Antibodies (immunoglobulins) bind to pathogens and kill them. There is currently no cure or treatment for celiac disease. Many studies are being conducted on new treatments. For the time being, a gluten-free diet can help to mend the intestinal lining or villi and alleviate symptoms.

REFERENCES

- [1] Iversen R, Sollid LM. The immunobiology and pathogenesis of celiac disease. Annual Review of Pathology: Mechanisms of Disease. 2023 Jan 24;18:47-70.
- [2] AndrénAronsson C, Agardh D. Intervention strategies in early childhood to prevent celiac disease—a minireview. Frontiers in Immunology. 2023 Feb 22;14:1106564.
- [3] Auricchio R, Troncone R. Can celiac disease be prevented?. Frontiers in Immunology. 2021 May 14;12:672148.
- [4] Quarpong W, Card TR, West J, Solaymani-Dodaran M, Logan RF, Grainge MJ. Mortality in people with coeliac disease: long-term follow-up from a Scottish cohort. United European Gastroenterology Journal. 2019 Apr;7(3):377-87.
- [5] Parzanese I, Qehajaj D, Patrinicola F, Aralica M, Chiriva-Internati M, Stifter S, Elli L, Grizzi F. Celiac disease: From pathophysiology to treatment. World journal of gastrointestinal pathophysiology. 2017 May 5:8(2):27.
- [6] Green PH, Cellier C. Celiac disease. New england journal of medicine. 2007 Oct 25;357(17):1731-43.
- [7] Secretariat MA. Clinical utility of serologic testing for celiac disease in asymptomatic patients: an evidence-based analysis. Ontario Health Technology Assessment Series. 2011;11(3):1.
- [8] Alharbi IS, Sweid AM, Memon MY, Alshieban S, Alanazi A. Correlation of TTG IgA level with small intestinal histopathological changes for celiac disease among adult Saudi patients. Journal of Translational Internal Medicine. 2020 May 9;8(1):48-53.
- [9] Hemati N, Sadeghi M. Plasma citrulline levels in patients with celiac disease: a meta-analysis of case-control studies. J. Res. Med. Dent. Sci. 2018 Feb 1;6(1):397.
- [10] Birot S, Madsen CB, Kruizinga AG, Christensen T, Crépet A, Brockhoff PB. A procedure for grouping food consumption data for use in food allergen risk assessment. Journal of Food Composition and Analysis. 2017 Jun 1;59:111-23.
- [11] Gumienna M, Górna B. Gluten hypersensitivities and their impact on the production of gluten-free beer. European Food Research and Technology. 2020 Nov;246(11):2147-60.
- [12] Tio M, Cox MR, Eslick GD. Meta-analysis: coeliac disease and the risk of all-cause mortality, any malignancy and lymphoid malignancy. Alimentary pharmacology & therapeutics. 2012 Mar;35(5):540-51.
- [13] Holmes, G.K.T. Muirhead, A. Mortality in coeliac disease: a population-based cohort study from a single centre in Southern Derbyshire, UK BMJ Open Gastroenterol, 5 2018, Article e000201.
- [14] Lebwohl, B. Green, P.H.R Söderling, J. *et al.* Association between celiac disease and mortality risk in a Swedish population JAMA, 323 2020, pp. 1277-1285.
- [15] Koskinen, I. Virta, L.J. Huhtala, H. *et al.* Overall and cause-specific mortality in adult celiac disease and dermatitis herpetiformis diagnosed in the 21st century Am J Gastroenterol, 115 2020, pp. 1117-1124.
- [16] Abdul Sultan, A. Crooks, C.J. Card, T. *et al.* Causes of death in people with coeliac disease in England compared with the general population: a competing risk analysis Gut, 64 2015, pp. 1220-1226.
- [17] Hervonen, K. Alakoski, A. Salmi, T.T. *et al.* Reduced mortality in dermatitis herpetiformis: a population-based study of 476 patients Br J Dermatol, 167 2012, pp. 1331-1337.
- [18] Lohi, S. Mäki, M. Rissanen, H. *et al.* Prognosis of unrecognized coeliac disease as regards mortality: a population-based cohort study Ann Med, 41 2009, pp. 508-515.
- [19] Godfrey, J.D. Brantner, T.L. Brinjikji, W. et al. Morbidity and mortality among older individuals with undiagnosed celiac disease Gastroenterology, 139 2010, pp. 763-769.

- [20] Kårhus, L.L. Skaaby, T. Petersen, J. *et al.* Long-term consequences of undiagnosed celiac seropositivity Am J Gastroenterol, 115 2020, pp. 1681-1688.
- [21] Ludvigsson, J.F., Montgomery, S.M. Ekbom, A. *et al.* Small-intestinal histopathology and mortality risk in celiac disease JAMA, 302 2009, pp. 1171-1178.
- [22] Koskinen, I. Hervonen, K. Pukkala, E. *et al.* Cancer incidence and factors associated with malignancies in coeliac disease during long-term follow-up GastroHep, 3 2021, pp. 107-115.
- [23] Kurppa, K. Lauronen, O. Collin, P. *et al.* Factors associated with dietary adherence in celiac disease: a nationwide study Digestion, 86 2013, pp. 309-314.
- [24] See, J.A. Kaukinen, K. Makharia, G.K. *et al.* Practical insights into gluten-free diets Nat Rev GastroenterolHepatol, 12 2015, pp. 580-591.
- [25] Ilus, T. Kaukinen, K. Virta, L.J. *et al.* Incidence of malignancies in diagnosed celiac patients: a population-based estimate Am J Gastroenterol, 109 2014, pp. 1471-1477.
- [26] Rispo, A. Imperatore, N. Guarino, M. *et al.* Metabolic-associated fatty liver disease (MAFLD) in coeliac disease. Liver Int, 41 2021, pp. 788-798.
- [27] Schneider, C.V. Kleinjans, M. Fromme, M. *et al.*Phenome-wide association study in adult coeliac disease: role of HLA subtype Aliment PharmacolTher, 53 2021, pp. 510-518.
- [28] Reilly, N.R., Lebwohl, B. Hultcrantz, R. et al. Increased risk of non-alcoholic fatty liver disease after diagnosis of celiac disease J Hepatol, 62 2015, pp. 1405-1411.
- [29] Osman, D. Umar, S. Muhammad, H *et al.* Neurological manifestation of coeliac disease with particular emphasis on gluten ataxia and immunological injury: a review article GastroenterolHepatol Bed Bench, 14 2021, pp. 1-7.