Review Article **ISSN: 2349 – 7106**

Asian Journal of Research in Chemistry and Pharmaceutical Sciences

Journal home page: www.ajrcps.com

https://doi.org/10.36673/AJRCPS.2024.v12.i02.A07

A REVIEW ON CELIAC DISEASE

Karra Geetha[*1], M. Bala Tripura Sundari[2], Vemula Sowmya[2], Duggireddy Navya Sree[2]

[1*]Department of Pharmaceutics, CMR College of Pharmacy, Hyderabad, Telangana, India.
[2]Department of Pharmacology, CMR College of Pharmacy, Hyderabad, Telangana, India.

ABSTRACT

Celiac disease, often called "celiac sprue," is a chronic inflammatory disorder of small intestinal that arises on exposure to gluten dietary products in susceptible individuals. The chance of getting celiac disease can be raised by a number of conditions, such as diabetes (type 1), Crohn's disease, down syndrome and Addison's disease. There are a lot of contributing factors to this condition, both environmental and inherited. While the major histocompatibility complex region has been shown to be a genetic predisposition, gluten is an environmental trigger. 1% of people worldwide suffer from celiac disease. The main reason it goes unrecognized is that about half of individuals afflicted don't show the gastrointestinal symptoms instead, they show other indications of deficiency in calories or do not show symptoms at all. In this article, we review the recent data regarding the pathology, clinical indications, available tests for diagnosis, and management of celiac disease by various treatment methods.

KEYWORDS

Celiac disease, Gluten, Pathogenesis, Diagnostic methods and Treatment of celiac disease.

Author for Correspondence:

Karra Geetha,

Department of Pharmaceutics,

CMR College of Pharmacy,

Hyderabad, Telangana, India.

Email: geetabiokarra@gmail.com

INTRODUCTON

Celiac disease is an autoimmune disorder caused by an abnormal adaptive response of immune system in susceptible individuals allergic to gluten-containing foods[1]. Celiac disease was first defined in 1888 by Samuel Gee[2,3]. In celiac disease patients due to gluten ingestion it causes mucosal impairment surface and enteropathy[4-7]. It can also lead to various multiple diseases in humans.

In comparison to other autoimmune diseases, celiac disease has special properties, such as complete recovery of mucosal injury and disease severity can be reversed by avoiding gluten exposure. It is now classified as undetected celiac disease can have

catastrophic consequences for both adult and young patients[8-11].

It is an immune-triggered systemic disorder by gluten intake in some individuals, occurring in genetically predisposed individuals. Gluten is an insoluble protein of cereal, including Prolamins found in

Gliadin (wheat),

Secalins (rye),

Hordein (barley)[12-20].

Gluten: The environmental trigger for the cause of celiac disease

Gluten has viscoelastic qualities which are important for dough creation to give to bread from wheat flour which has define texture and flavor which is widely used for manufacturing various food items. Gluten is applicable in various food industries due to its different properties, the food items manufactured from gluten are bread, cookies and pasta but also used in sauces, quick soups and even in pharma industry as a hidden product. As a result, the gluten intake is ranging from 15-20grams per day in western countries, the gluten containing diet is high in most of the countries. Patients with celiac disease have to follow a strict gluten-free diet[21-23]. The daily intake of more than 10-50mg of gluten can cause histological abnormalities. The celiac disease patients were advised to lower their gluten intake to 10-50mg per daily[24-26].

Gluten is mixture of various gliadin's and glutenin's, which are found in wheat, barley and rye. Three main types of gliadin's are α,γ,ω, low and high molecular weight glutenin's. Gluten consist of high content of amino acids glutamine of 30% and proline of 15%. The proline content makes gluten highly resistant to gastro-intestinal enzymes degradation, which make them large immunogenic gluten peptides to mucosal layer surface. It also has high in nitrogen content due to it high levels of glutamine which is required for seed germination. The modern wheat variety consist of three complete genomes of gliadins and glutenin's and up to 100 different gluten proteins in single wheat variety which may pose threat for pathogenesis of celiac disease[21,22].

Gluten is absorbed poorly from the human gut in normal healthy individual (with or without celiac disease). The peptides of gluten can pass through small intestines submucosa. The human enzyme transglutaminase 2 (also known as tissue transglutaminase {tTG}) will help in deamidation of gluten peptides in small intestine, which has high binding capacity to human leucocyte antigen HLA DQ8 and HLA DQ2 molecules as a result it acts as a triggering factor for inflammation in celiac disease patients[27,28].

Other than gluten various environmental factors are responsible for pathogenesis of celiac disease[29,30]. The life events also influence the intestinal environment such as breast-feeding after delivery and other habits which alter gut health and gut microbiota. According to research the children's suffering from gastrointestinal infections from are a risk of developing celiac disease in future[32].

The gliadins proteins are permeable between epithelial enterocytes to lamina propria and it may activate transglutaminase and enhance interferon production[31,33-35].

Effect of microbiome on celiac disease

Most of the studies have been done on microbiome in celiac patients, most of the studies focused on certain species like Bifidobacterium and Lactobacillus in gut microbial concentrations in celiac disease patients. The results observed that patient with this disease have increased concentration of gram-negative bacteria mostly proteobacteria. *In-vitro* studies reveal that patients with celiac disease can lead to modification of mucosal barrier and prolonged immune activation or sensitization for activation of gliadin causing symptoms clinically. Gluten-free diet is only treatment for celiac disease, to normalize the microbiome in patients the use of probiotics can be beneficial. Treatment with Bifidobacterium or Lactobacterium can help in restoring the altered gut microbiome and immune activation[36].

Celiac disease is a female predominant disease according to the studies. According to the Italian studies women had more symptoms, Lower body weight and severe anemia. Iron- deficiency anemia and lower serum cholesterol are common problem

for celiac disease patients. As autoimmune disorder usually has female predominance than male[37].

Symptoms

The Gastro intestinal symptoms of celiac disease are:

Nausea and vomiting
Stools of pale color with foul smell
Pain in the abdominal region
Diarrhea
Constipation
Fatty stools that float
Bloating, gas[38-44].

Celiac Disease related disorders

Digestive disorders

Irregular bowl movement
Diarrhea for longer period of time
Irregular occurrence of stools
Malabsorption of nutrients
Vomiting
Pain in the abdomen
Anorexia
Constipation that is chronic (mostly seen in children's)
Low weight gain
Reduced appetite

Extra-digestive disorders

Delay in puberty
Tooth enamel hypoplasia
Fatigue for longer time
Iron deficiency
Vitamin deficiency
Retardation of growth
Dermatitis
Liver cytolysis
Early Menopause
Pain in bones
Fractures
Osteopenia, Osteoporosis
Neuropathy

Associated pathologies

Williams syndrome
First degree Celiac disease
Diabetes (type 1)
Down syndrome
Deficiency of IgA
CVID (common variable immune deficiency)
Sjogren syndrome
Autoimmune disorders
Corhn's disease
Neurological disorders
Turner syndrome[45-55].

CELIAC DISEASE AND CONCOMITANT CONDITIONS

Celiac disease with nutritional deficiencies

As celiac disease is characterized by malabsorption, weight loss, vitamin and mineral deficiencies. The celiac disease patients are at a risk of vitamin and mineral deficiencies like calcium, copper, folate, folate and zinc. The untreated celiac disease experienced vitamin B12 deficiency, anemia, iron deficiency and zinc deficiency[56].

Celiac disease with rheumatoid arthritis

There is a physiology overlap between celiac disease and rheumatoid arthritis, as they both are autoimmune disorders. Rheumatoid arthritis (RA) affect the joints and celiac disease (CD) affect small intestine. RA is related to human leukocyte antigen HLA DRB1 and CD is related to HLA DQ2 and D haplotypes. The autoantibodies which is commonly found in CD, other name is immunoglobulin G anti-gliadin antibodies (IgG AGA) was found in some patients with RA disease[57].

Celiac disease with sepsis

Celiac disease increases the permeability of the intestine as well as impaired functioning of mucosal barrier. Due to exposed to gluten individuals and weaker spleen there is increased mortality from streptococcal, pneumococcal and gram-negative bacteria infection. As this can lead to sepsis[58].

Celiac disease with risk of Hodgkin's lymphoma

Celiac disease patients are at risk of malignancy, the exact mechanism is unknown. It is thought that combination of inflammatory cytokines, prolonged antigenic stimulation, chronic inflammation and increased permeability. Regardless of their diet CD patients are nine times more likely to develop non-Hodgkin's lymphoma (NHL)[59].

Celiac disease vs inflammatory bowel disease (IBD)

Celiac disease patients had mostly diagnosed with Crohn's disease, ulcerative colitis, IBD as they

common symptoms such as weight loss, abdomen pain and diarrhea and pathology is also similar to celiac disease[60].

Celiac disease with thyroid disorders

CD patients due to gluten intake there is release of antibodies which is also found to increased levels of thyroid-related and antiphospholipid autoantibodies[61].

PATHOGENESIS

Celiac disease is caused by the both environmental and genetic factors. Many research studies have been done to study genetic and immunological causes of celiac disease in recent years. In normal conditions epithelia is impermeable to macromolecules such as gliadin.

In celiac disease the permeability is increased and causes the disruption of tight junction (TJ) systems integrity. The increased permeability across the endothelium and epithelial layers cause breach in intestinal barrier functions is caused by celiac disease[62-64].

By the interaction of three genes, environment, gluten according to (Figure No.1). The predisposing factors responsible for celiac disease are two HLA class II genes: HLA-DQ8 (DQA1*03-DQB1*0302) and HLA-DQ2 (DOA1*05-DQB1*02).

Other non-HLA genes can also contribute for the development of celiac disease but HLA-DQ8 and HLA-DQ2 are virtually present in all celiac disease patients[65,66].

Different types of celiac disease

Asymptomatic celiac disease

In this type of celiac disease symptoms are not observed as mentioned above symptoms even at diagnosis, patients do not exhibit any reactions to gluten or gluten removal which makes the diagnosis difficult[67-80].

Typical celiac disease

It is defines as gluten induced enteropathy by symptoms and signs. Malabsorption or malabsorption syndrome, diarrhea, weight loss, steatorrhoea, oedema owing to hypoalbuminemia[81].

Atypical celiac disease

It is also gluten-induced enteropathy but symptoms like weight loss and other symptoms and signs were not observed. Extraintestinal signs were observed like metabolic disease or symptoms[82-84].

Classical celiac disease

It is characterized by symptoms and signs such as malabsorption, weight loss, defects in growth, steatorrhoea are all were recorded in this type[85-93].

Non- classical celiac disease

No symptoms and signs of malabsorption were observed in celiac disease patients[28].

Silent celiac disease

It correlate with asymptomatic celiac disease, hence silent name can be added as no signs and symptoms were observed[28].

Sub-clinical celiac disease

This is less detected type of celiac disease, no signs and symptoms were observed but they have laboratory signs such as anemia, liver abnormalities in liver biomarkers in function tests, enamel defects, osteoporosis, other endoscopic findings[94-98].

Symptomatic celiac disease

By the name itself we can define this type as clinically noticeable symptoms can be seen in reaction to gluten such as gastrointestinal and extraintestinal symptoms[99-108].

Overt celiac disease

Clinically gluten related symptoms are observed such as gastrointestinal (diarrhea, bloating) and extraintestinal symptoms such as neurological symptoms and exhaustion[109,110.]

Refectory celiac disease

It is defined as chronic or recurring symptoms and signs of malabsorption associated with villous atrophy (VA)[111-119].

Latent celiac disease

There are many definitions of latent celiac disease, in this type patients will get positive serology celiac disease with normal mucosa or absence of villous atrophy, it can also lead to other autoimmune diseases[120-122].

Potential celiac disease

They are detected positive to celiac serology test with a risk of developing intestine mucosa related issues[123].

Differential diagnosis

Malabsorption and villous atrophy are symptoms of celiac disease. Other disorders, however, can induce

significant villi flattening and increased intraepithelial lymphocytes (IEL). Differential diagnosis is especially important in people with CD who have negative serology. The following list of diseases, which may exhibit similar signs and symptoms.

Graft-vs- host disease Viral enteritis
Tropical sprue
Carbohydrate intolerance
Collagenous colitis
Giardiasis
Acquired immunodeficiency syndrome
Crohn's disease of small intestine
Autoimmune enteropathy
Small intestinal lymphoma
Cow's milk intolerance[124].

DIAGNOSIS

If IgA anti transglutaminase antibodies are detected then it confirms the presence of celiac disease and it is preferred for above 2 years age patients it has high level of evidence for proving disease.

IgG based detection, it has to be conducted in low IgA patients, it is strongly recommended with moderate level of evidence

Serological tests can be performed, if they are negative then intestinal biopsy should be performed on gluten-free patients.

Antibody test against gliadin is not suggested for primary test detection of celiac test.

Combining various celiac disease tests in replacement of TTG IgA test.

while screening children's below 2 years of age for celiac disease IgA and IgG tests has to be considered.

CONFIRMATORY TESTS FOR CELIAC DISEASE

This disease has to be confirmed based on medical history observation, serology test, physical examination, endoscopy.

Endoscopy of small intestine is important for patients with suspected celiac disease to confirm the diagnosis.

Duodenal biopsy is also recommended for confirming celiac disease[125].

Treatment for celiac disease

The most effective treatment of celiac disease is to follow a gluten-free diet for life-long. Avoid gluten and gluten containing foods and pharmaceuticals which are derived from barley, wheat and rye.

Gluten-free diet

Patient is not allowed to take gluten products and gluten related products as they cause serious effects such as grains, starch, barley, barley, malt, wheat.

Monitoring

Lifelong they have to adhere to the gluten-free diet as it is best way to reduce the risk of other diseases and it also improves the quality of life. It is easy to manage in this way as it results in reducing the risk of celiac disease and other malignant diseases and other autoimmune diseases

Laboratory assessment

Specific serological tests can performed to check the progression of disease ad the frequency of testing will be depending up on the time spent on gluten free diet. According to resent studies IgA and IgG tests are best way to detect compliance as they can detect small dietary infractions[126].

Anti-inflammatory compounds

Inflammation is the main sign as it is autoimmune disorder or due to use of corticosteroids and immunosuppressants medications. Hence administration of topically active medications for celiac disease may be beneficial[127].

Detoxification by probiotic bacteria

Celiac disease is related with changes in the gut bacteria which may leads to disease development. There are certain bacteria which is identified in celiac disease patients in cell cultures hence they can be treated using probiotics and increasing the gut health.

Enzyme supplementation therapy

The enzyme supplement therapy can be an option for celiac patients as they breakdown gliadin and other prolamins. The enzymes responsible for gluten digestion has yet to found and it can serve as great replacement therapy for celiac disease[128].

Surgery

In obese celiac patients the surgeries can be safe, if diet is not helpful as it boosts weight loss and decreases the chances of death[129].

Prevention of celiac disease

According to the study it states that newborn of celiac parents as they are high susceptible of developing celiac disease as they are in risk group. Not only gut health and genes cause celiac disease but also some kind of viruses can also cause celiac disease. The gastrointestinal infections can also lead to celiac disease.

Rota virus vaccination have great preventive measure of reducing the risk of developing celiac disease. Lowering the exposure to gluten containing food from childhood onwards (from 6 month of age) can be a peventive method. Ongoing genomic, environment, microbiome and metabolic studies in celiac disease aim to identify potential primary prevention targets by identifying the microbiome, metabolic and environmental factors responsible for loss of gluten tolerance, thus translating genetic predisposition in to clinical outcome[130].

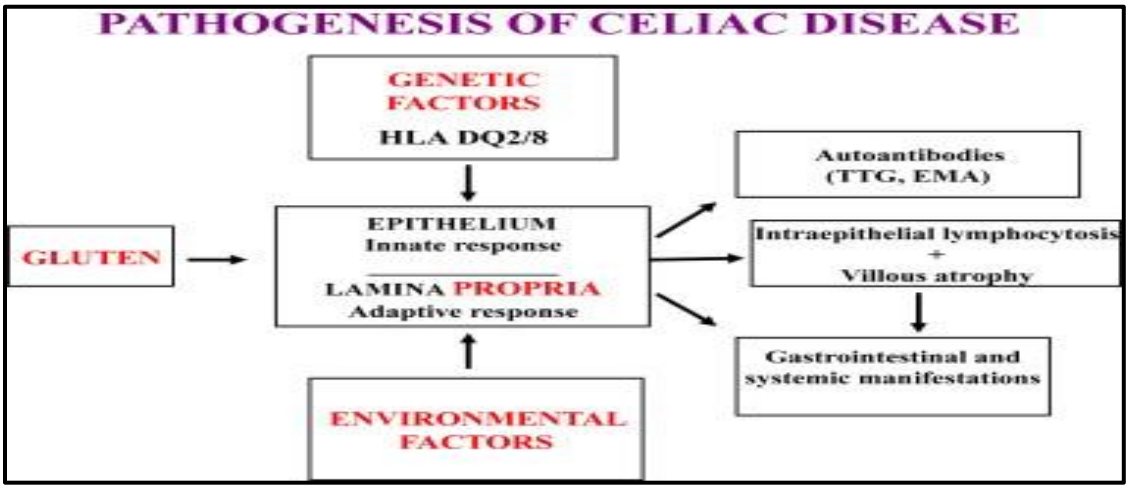

Figure No.1: Pathogenesis of celiac disease

CONCLUSION

Celiac disease is a chronic inflammatory, autoimmune intestinal illness caused by gluten indigestion in people who are genetically predisposed to it. This condition is caused by environmental factors and produces inflammation in the small intestine, which can lead to nutrient malabsorption. It may operate as a risk factor for a variety of intestinal ailments as well as extra-intestinal disorders such as vitamin deficiencies.

This disease's diagnosis can be difficult because it shares many characteristics with other intestinal ailments; nonetheless, several diagnostic approaches are available based on the intensity with which it can be treated. The gluten-free diet is the most effective treatment, and several novel therapeutic techniques are being tested. To avoid problems, early diagnosis and treatment are critical.

AUTHORS CONTRIBUTION

All the authors mentioned in the article have equal participation in data collection, investigation, conceptualization, data analysis, data validation, review and editing.

ACKNOWLEDGEMENT

The authors wish to express their sincere gratitude to Department of Pharmaceutics, CMR College of Pharmacy, Hyderabad, Telangana, India for providing the necessary facilities to carry out this review work.

CONFLICTS IF INTEREST

All authors declare that they have no conflicts of interest and therefore nothing to declare.

BIBLIOGRAPHY

1. Losowsky M S. A history of coeliac disease, *Digestive Diseases*, 26(2), 2008, 112-120.
2. Dicke W K, Weijers H A, Kamer J V. Coeliac disease the presence in wheat of a factor having a deleterious effect in cases of coeliac disease, *Acta Paediatrica*, 42(1), 1953, 34-42.
3. Elli L, Branchi F, Tomba C, Villalta D, Norsa L, Ferretti F, Roncoroni L, Bardella M T. Diagnosis of gluten related disorders: Celiac disease, wheat allergy and non-celiac gluten sensitivity, *World Journal of Gastroenterology: WJG*, 21(23), 2015, 7110.
4. Fasano A, Catassi C. Current approaches to diagnosis and treatment of celiac disease: An evolving spectrum, *Gastroenterology*, 120(3), 2001, 636-651.
5. Green P H, Lebwohl B, Greywoode R. Celiac disease, *Journal of Allergy and Clinical Immunology*, 135(5), 2015, 1099-1106.
6. Assimakopoulos S F, Papageorgiou I, Charonis A. Enterocytes' tight junctions: From molecules to diseases, *World J Gastrointest Pathophysiol*, 2(6), 2011, 123-137.
7. Jeon M K, Klaus C, Kaemmerer E, Gassler N. Intestinal barrier: Molecular pathways and modifiers, *World J Gastrointest Pathophysiol*, 4(4), 2013, 94-99.
8. Rubio-Tapia A, Kyle R A, Kaplan E L, Johnson D R, Page W, Erdtmann F, Brantner T L, Kim W R, Phelps T K, Lahr B D, *et al*. Increased prevalence and mortality in undiagnosed celiac disease, *Gastroenterology*, 137(1), 2009, 88-93.
9. Holmes S. Coeliac disease: Symptoms, complications and patient support, *Nurs Stand*, 24(35), 2010, 505-506.
10. Norstrom F, Lindholm L, Sandstrom O, Nordyke K, Ivarsson A. Delay to celiac disease diagnosis and its implications for health-related quality of life, *BMC Gastroenterol*, 11, 2011, 118.
11. Ilaria Parzanese, Dorina Qehajaj, Federica Patrinicola, Merica Aralia, Maurizio Chiriva-Internati, Sanja Stifter, Luca Elli, Fabio Grizzi. Celiac disease: From pathophysiology to treatment, *World J Gastrointest Pathophysiol*, 8(2), 2017, 27-38.
12. Troncone R, Auricchio S. Rotavirus and celiac disease: Clues to the pathogenesis and perspectives on prevention, *J Pediatr Gastroenterol Nutr*, 44(5), 2007, 527-528.
13. Troncone R, Jabri B. Coeliac disease and gluten sensitivity, *J Intern Med*, 269(6), 2011, 582-590.
14. Stene L C, Honeyman M C, Hoffenberg E J, Haas J E, Rewers M. Rotavirus infection frequency and risk of celiac disease autoimmunity in early childhood: Alongitudinal study, *Official Journal of the American College of Gastroenterology, ACG*, 101(10), 2006, 2333-2340.
15. Pinier M, Fuhrmann G, Verdu E F, Leroux J C. Prevention measures and exploratory pharmacological treatments of celiac disease, *Am J Gastroenterol*, 105(12), 2010, 2551-2561.
16. Catassi C, Fabiani E, Iacono G, Volta U, Accomando S, Picarelli A, De Vitis I, *et al*. A prospective, double-blind, placebo-controlled trial to establish a safe gluten threshold for patients with celiac disease, *Am J Clin Nutr*, 85(1), 2007, 160-166.

17. Silano M, Agostoni C, Guandalini S. Effect of the timing of gluten introduction on the development of celiac disease, *World J Gastroenterol,* 16(16), 2010, 1939-1942.
18. Sanz Y, De Pama G, Laparra M. Unraveling the ties between celiac disease and intestinal microbiota, *Int Rev Immunol,* 30(4), 2011, 207-218.
19. Elli L, Rossi V, Conte D, Ronchi A, Tomba C, Passoni M, Bardella M T, Roncoroni L, Guzzi G. Increased mercury levels in patients with celiac disease following a gluten-free regimen, *Gastroenterol Res Pract,* 2015, Article Id: 953042, 2015, 6.
20. Lerner A, Matthias T. Possible association between celiac disease and bacterial transglutaminase in food processing: A hypothesis, *Nutr Rev,* 73(8), 2015, 544-552.
21. Shan L, Molberg O, Parrot I, Hausch F, Filiz F, Gray G M, Sollid L M, Khosla C. Structural basis for gluten intolerance in celiac sprue, *Science,* 297(5590), 2002, 2275-2279.
22. Shan L, Qiao S W, Arentz-Hansen H, Molberg O, Gray G M, Sollid L M, Khosla C. Identification and analysis of multivalent proteolytically resistant peptides from gluten: Implications for celiac sprue, *J Proteome Res,* 4(5), 2005, 1732-1741.
23. Tjon J M L, Van Bergen J, Koning F. Celiac disease: How complicated can it get? *Immunogenetics,* 62(10), 2010, 641-651.
24. Catassi C, Fabiani E, Iacono G, *et al*. A prospective, double-blind, placebo-controlled trial to establish a safe gluten threshold for patients with celiac disease, *Am J Clin Nutr,* 85(1), 2007, 160-166.
25. Selby W S, Painter D, Collins A, Faulkner-Hogg K B, Loblay R H. Persistent mucosal abnormalities in coeliac disease are not related to the ingestion of trace amounts of gluten, *Scand J Gastroenterol,* 34(9), 1999, 909-914.
26. Cohen I S, Day A S, Shaoul R. Gluten in celiac disease-more or less? *Rambam Maimonides Med J,* 10(1), 2019, e0007.
27. Molberg O, Mcadam S N, Korner R, Quarsten H, Kristiansen C, Madsen L, Fugger L, Scott H, Noren O, Roepstorff P, Lundin K E. Tissue transglutaminase selectively modifies gliadin peptides that are recognized by gut-derived T cells in celiac disease, *Nature Medicine,* 4(6), 1998, 713-717.
28. Ludvigsson J F, Kaukinen K, Kelly C P, Leonard J N, Lundin K E. The Oslo definitions for coeliac disease and related terms, *Gut,* 62(1), 2013, 43-52.
29. Tanpowpong P, Camargo C A. Early-life vitamin D deficiency and childhood onset coeliac disease, *Public Health Nutr,* 17(4), 2014, 823-826.
30. Lebwohl B, Murray J A. Season of birth in a nationwide cohort of coeliac disease patients, *Arch Dis Child,* 98(1), 2013, 48-51.
31. Peter H R. Green M D, Benjamin Lebwohl M D, Ruby Greywoode M D. Celiac disease, *The Journal of Allergy and Clinical Immunology,* 135(5), 2015, 1099-1106.
32. Riddle M S, Murray J A, Cash B D, Pimentel M, Porter C K. Pathogen-specific risk of celiac disease following bacterial causes of foodborne illness: A retrospective cohort study, *Dig Dis Sci,* 58(11), 2013, 3242-3245.
33. Welander A, Ludvigsson J, Ludvigsson J F. Infectious disease and risk of later celiac disease in childhood, *Pediatrics,* 125(3), 2010, e530-536.
34. Holm S, Andersson Y, Gothefors L, Lindberg T. Increased protein absorption after acute gastroenteritis in children, *Acta Paediatr,* 81(8), 1992, 585-588.
35. Stene L C, Honeyman M C, Sokol R J, Emery L, *et al*. Rotavirus infection frequency and risk of celiac disease autoimmunity in early childhood: A longitudinal study, *Am J Gastroenterol,* 101(10), 2006, 2333-2340.
36. Kristensen N B, Allin K H, *et al*. Alterations in fecal microbiota composition by probiotic supplementation in healthy adults: A systematic review of randomized controlled trials, *Genome Med,* 8(1), 2016, 52.

37. Bai D, Brar P, Holleran S, Ramakrishnan R, Green P H. Effect of gender on the manifestations of celiac disease: Evidence for greater malabsorption in men, *Scandinavian Journal of Gastroenterology,* 40(2), 2005, 183-187.
38. Kagnoff M F. AGA institute medical position statement on the diagnosis and management of celiac disease, *Gastroenterology,* 131(6), 2006, 1977-1980.
39. Sanders D S, Hurlstone D P, Stokes R O, *et al*. Changing face of adult coeliac disease: experience of a single university hospital in South York-shire, *Postgrad Med J,* 78(915), 2002, 31-33.
40. Collin P. Should adults be screened for celiac disease? What are the benefits and harms of screening? *Gastroenterology,* 128(4-1), 2005, S104-S108.
41. Green P H. The many faces of celiac disease: Clinical presentation of celiac disease in the adult population, *Gastroenterology,* 128(4-1), 2005, S74-S78.
42. Dewar D H, Ciclitira P J. Clinical features and diagnosis of celiac disease, *Gastroenterololology,* 128(4-1), 2005, S19-S24.
43. Bode S, Gudmand-Hoyer E. Symptoms and haematologic features in consecutive adult coeliac patients, *Scand J Gastroenterol,* 31(1), 1996, 54-60.
44. John Presutti R, John R Cangemi, Harvey D Cassidy, David A Hill. Celiac disease, *Am Fam Physician,* 76(12), 2007, 1795-1802.
45. Godat S, Velin D, Aubert V, Nydegger A, Schoepfer A M, Maillard M H. An update on celiac disease, *Revue Medicale Suisse,* 9(396), 2013, 1584-1589.
46. Hill I D, Hoffenberg E J, Horvath K, Murray J A, Pivor M, Seidman EG. Guideline for the diagnosis and treatment of celiac disease in children: Recommendations of the North American Society for pediatric gastroenterology, *Hepatology and Nutrition, Journal of Pediatric Gastroenterology and Nutrition,* 40(1), 2005, 1-9.
47. Mouterde O, Hariz M B, Dumant C. Le nouveau visage de la maladie cœliaque, *Archives De Pediatrie,* 15(5), 2008, 501-503.
48. Fasano A. Clinical presentation of celiac disease in the pediatric population, *Gastroenterology,* 128(4), 2005, S68-73.
49. Rashid M, Lee J. Serologic testing in celiac disease: Practical guide for clinicians, *Canadian Family Physician,* 62(1), 2016, 38-43.
50. Kelly C P, Bai J C, Liu E, Leffler D A. Advances in diagnosis and management of celiac disease, *Gastroenterology,* 148(6), 2015, 1175-1186.
51. Nion-Larmurier I, Cosnes J. Celiac disease, *Gastroenterologie Clinique Et Biologique,* 33(6-7), 2009, 508-517.
52. Bushara K O. Neurologic presentation of celiac disease, *Gastroenterology,* 128(4), 2005, S92-97.
53. Nenna R, Petrarca L, Verdecchia P, Florio M, Pietropaoli N, Mastrogiorgio G, Bavastrelli M, Bonamico M, Cucchiara S. Celiac disease in a large cohort of children and adolescents with recurrent headache: A retrospective study, *Digestive and Liver Disease,* 48(5), 2016, 495-498.
54. Parisi P, Pietropaoli N, Ferretti A, Nenna R, Mastrogiorgio G, Del Pozzo M, Principessa L, Bonamico M, Villa M P. Role of the gluten-free diet on neurological-EEG findings and sleep disordered breathing in children with celiac disease, *Seizure,* 25, 2015, 181-183.
55. Ben Houmich T, Admou B. Celiac disease: Understandings in diagnostic, nutritional and medicinal aspects, *International Journal of Immunopathology and Pharmacology,* 35, 2021.
56. Dahele A, Ghosh S. Vitamin B12 deficiency in untreated celiac disease, *Am J Gastroenterol,* 96(3), 2001, 745-750.
57. Lerner A, Matthias T. Rheumatoid arthritis-celiac disease relationship: Joints get that gut feeling, *Autoimmun Rev,* 14(11), 2015, 1038-1047.

58. Tjemberg A R, Bonnedahl J, Ludvigsson J F. Does celiac disease influence survival in sepsis? A nationwide longitudinal study, *PLoS One,* 11(4), 2016, e0154663.
59. Green P H, Fleischauer A T, Bhagat G, Goyal R, Jabri B, Neugut A l. Risk of malignancy in patients with celiac disease, *Am J Med,* 115(3), 2003, 191-195.
60. Casella G, D'Inca R, Oliva L, *et al*. Prevalence of celiac disease in inflammatory bowel diseases: An IG-IBD multi-centre study, *Dig Liver Dis,* 42(3), 2010, 175-178.
61. Sattar N, Lazare F, Kacer M, *et al*. Celiac disease in children, adolescents and young adults with autoimmune thyroid disease, *J Pediatr,* 158(2), 2011, 272-275.
62. Fasano A. Zonulin and its regulation of intestinal barrier function: The biological door to inflammation, autoimmunity and cancer, *Physiological Reviews,* 91(1), 2011, 151-175.
63. Clemente M G, Congia M, Fasano A. Early effects of gliadin on enterocyte intracellular signalling involved in intestinal barrier function, *Gut,* 52(2), 2003, 218-223.
64. Lionetti E, Catassi C. New clues in celiac disease epidemiology, pathogenesis, clinical manifestations and treatment, *Inter Rev of Immu,* 30(4), 2011, 219-231.
65. West J, Logan R F, Hill P G, Lloyd A, Lewis S, Hubbard R, Reader R, Holmes G K, Khaw K T. Seroprevalence, correlates, and characteristics of undetected coeliac disease in *England. Gut,* 52(7), 2003, 960-965.
66. Mustalahti K, Catassi C, Metzger M H, Maki M. The prevalence of celiac disease in Europe: results of a centralized, international mass screening project, *Annals of Medicine,* 42(8), 2010, 587-595.
67. Katz K D, Rashtak S, Murray J A. Screening for celiac disease in a North American population: Sequential serology and gastrointestinal symptoms, *Official Journal of the American College of Gastroenterology, ACG,* 106(7), 2011, 1333-1339.
68. Tursi A, Elisei W, Gaspardone A, Lecca P G, Di Cesare L, Brandimarte G. Prevalence of celiac disease and symptoms in relatives of patients with celiac disease, *European Review for Medical and Pharmacological Sciences,* 14(6), 2010, 567-572.
69. Freeman H J. Risk factors in familial forms of celiac disease, *World Journal of Gastroenterology: WJG,* 16(15), 2010, 1828-1831.
70. Legroux-Gerot I, Leloire O, Blanckaert F, Tonnel F, Grardel B, Ducrocq J L, Cortet B. Screening for celiac disease in patients with osteoporosis, *Joint Bone Spine,* 76(2), 2009, 162-165.
71. Barker J M, Liu E. Celiac disease: Pathophysiology, clinical manifestations and associated autoimmune conditions, *Advances in Pediatrics,* 55(1), 2008, 349-365.
72. Alzahrani A S, Al Sheef M. Severe primary hyperparathyroidism masked by asymptomatic celiac disease, *Endocrine Practice,* 14(3), 2008, 347-350.
73. Ch'ng C L, Jones M K, Kingham J G. Celiac disease and autoimmune thyroid disease, *Clinical Medicine and Research,* 5(3), 2007, 184-192.
74. Swigonski N L, Kuhlenschmidt H L, Bull M J, Corkins M R, Downs S M. Screening for celiac disease in asymptomatic children with Down syndrome: Cost-effectiveness of preventing lymphoma, *Pediatrics,* 118(2), 2006, 594-602.
75. Dube C, Rostom A, Sy R, Cranney A, Saloojee N, Garritty C, Sampson M, Zhang L, Yazdi F, Mamaladze V, Pan I. The prevalence of celiac disease in average-risk and at-risk Western European populations: A systematic review, *Gastroenterology,* 128(4), 2005, S57-67.
76. Kumar V, Rajadhyaksha M, Wortsman J. Celiac disease-associated autoimmune endocrinopathies, *Clinical Diagnostic Laboratory Immunology,* 8(4), 2001, 678-685.

77. Hoffenberg E J, Bao F, Sokol R J, Rewers M. Transglutaminase antibodies in children with a genetic risk for celiac disease, *The Journal of Pediatrics,* 137(3), 2000, 356-360.
78. Lorini R, Scaramuzza A, Vitali L, Antonietta Avanzini M, De Giacomo C, Severi F. Clinical aspects of coeliac disease in children with insulin-dependent diabetes mellitus, *Journal of Pediatric Endocrinology and Metabolism,* 9(1), 1996, 101-112.
79. Stewart J. Asymptomatic coeliac disease in adults, *Irish Medical Journal,* 67(15), 1974, 415-416.
80. Marine M, Fernandez-Banares F, Alsina M, Farre C, Cortijo M, Santaolalla R, Salas A, Tomàs M, Abugattas E, Loras C, Ordas I. Impact of mass screening for gluten-sensitive enteropathy in working population, *World Journal of Gastroenterology: WJG,* 15(11), 2009, 1331-1338.
81. Fasano A, Catassi C. Current approaches to diagnosis and treatment of celiac disease: An evolving spectrum, *Gastroenterology,* 120(3), 2001, 636-651.
82. Wierink C D, Van Diermen D E, Aartman I H, Heymans H S. Dental enamel defects in children with coeliac disease, *International Journal of Paediatric Dentistry,* 17(3), 2007, 163-168.
83. Bucci P, Carile F, Sangianantoni A, Lo Muzio L. Oral aphthous ulcers and dental enamel defects in children with coeliac disease, *Acta Paediatrica,* 95(2), 2006, 203-207.
84. Rubio-Tapia A, Murray J A. The liver in celiac disease, *Hepatology,* 46(5), 2007, 1650-1658.
85. Marsh M N. Gluten, major histocompatibility complex and the small intestine: A molecular and immunobiologic approach to the spectrum of gluten sensitivity (‘celiac sprue’), *Gastroenterology,* 102(1), 1992, 330-354.
86. Logan R F, Tucker G, Heading R C, Ferguson A. Changes in clinical features of coeliac disease in adults in Edinburgh and the Lothians 1960-79, *Br Med J (Clin Res Ed),* 286(6359), 1983, 95-97.
87. Farrell R J, Kelly C P. Diagnosis of celiac sprue, The American Journal of *Gastroenterology,* 96(12), 2001, 3237-3246.
88. Wahab P J, Meijer J W, Goerres M S, Mulder C J. Coeliac disease: Changing views on gluten-sensitive enteropathy, *Scandinavian Journal of Gastroenterology,* 37(236), 2002, 60-65.
89. Lo W, Sano K, Lebwohl B, Diamond B, Green P H. Changing presentation of adult celiac disease, *Digestive Diseases and Sciences,* 48(2), 2003, 395-398.
90. Mulder C J, Cellier C. Coeliac disease: Changing views, *Best Practice and Research Clinical Gastroenterology,* 19(3), 2005, 313-321.
91. Dewar D H, Ciclitira P J. Clinical features and diagnosis of celiac disease, *Gastroenterology,* 128(4), 2005, S19-24.
92. Fasano A, Catassi C. Coeliac disease in children, *Best Pract Res Clin Gastroenterol,* 19(3), 2005, 467-478.
93. Nachman F, Maurino E, Vazquez H, Sfoggia C, Gonzalez A, Gonzalez V, Del Campo M P, Smecuol E, Niveloni S, Sugai E, Mazure R. Quality of life in celiac disease patients: Prospective analysis on the importance of clinical severity at diagnosis and the impact of treatment, *Digestive and Liver Disease,* 41(1), 2009, 15-25.
94. Meloni G, Dore A, Fanciulli G, Tanda F, Bottazzo G F. Subclinical coeliac disease in schoolchildren from northern Sardinia, *The Lancet,* 353(9146), 1999, 37.
95. Corazza G R, Frisoni M, Treggiari E A, Valentini R A, Filipponi C, Volta U, Gasbarrini G. Subclinical celiac sprue Increasing occurrence and clues to its diagnosis, *Journal of Clinical Gastroenterology,* 16(1), 1993, 16-21.
96. Bottaro G, Cataldo F, Rotolo N, Spina M, Corazza G R. The clinical pattern of subclinical/silent celiac disease: An analysis on 1026 consecutive cases, The American *Journal of Gastroenterology,* 94(3), 1999, 691-696.

97. Moreno M L, Vazquez H, Sugai E, Mauriño E, Gomez J C, Bai J C. Stratification of bone fracture risk in patients with celiac disease, *Clinical Gastroenterology and Hepatology*, 2(2), 2004, 127-134.
98. Baccini F, Aloe Spiriti M A, Vannella L, Monarca B, Delle Fave G, Annibale B. Unawareness of gastrointestinal symptomatology in adult coeliac patients with unexplained iron-deficiency anaemia presentation, *Alimentary Pharmacology and Therapeutics*, 23(7), 2006, 915-921.
99. Koskinen O, Collin P, Korponay-Szabo I, Salmi T, Iltanen S, Haimila K, Partanen J, Maki M, Kaukinen K. Gluten-dependent small bowel mucosal transglutaminase 2–specific IgA deposits in overt and mild enteropathy coeliac disease, *Journal of Pediatric Gastroenterology and Nutrition*, 47(4), 2008, 436-442.
100. Tjon J M, Van Bergen J, Koning F. Celiac disease: how complicated can it get? *Immunogenetics*, 62(10), 2010, 641-651.
101. Ciacci C, Maiuri L, Russo I, Tortora R, Bucci C, Cappello C. Efficacy of budesonide therapy in the early phase of treatment of adult coeliac disease patients with malabsorption: an *in vivo/in vitro* pilot study, *Clinical and Experimental Pharmacology and Physiology*, 36(12), 2009, 1170-1176.
102. West J, Logan R F, Hill P G, Khaw K T. The iceberg of celiac disease: What is below the waterline? *Clinical Gastroenterology and Hepatology*, 5(1), 2007, 59-62.
103. Schuppan D, Kelly C P, Krauss N. Monitoring non-responsive patients with celiac disease, *Gastrointestinal Endoscopy Clinics*, 16(3), 2006, 593-603.
104. Holtmeier W, Caspary W F. Celiac disease, *Orphanet Journal of Rare Diseases*, 1(1), 2006, 1-8.
105. Lahdeaho M L, Haapala A M, Maki M. Celiac disease: From inflammation to atrophy: A long-term follow-up study, *Journal of Pediatric Gastroenterology and Nutrition*, 41(1), 2005, 44-48.
106. Karnam U S, Felder L R, Raskin J B. Prevalence of occult celiac disease in patients with iron-deficiency anemia: A prospective study, *Southern Medical Journal*, 97(1), 2004, 30-35.
107. Barera G, Bonfanti R, Viscardi M, Bazzigaluppi E, Calori G, Meschi F, Bianchi C, Chiumello G. Occurrence of celiac disease after onset of type 1 diabetes: A 6-year prospective longitudinal study, *Pediatrics*, 109(5), 2002, 833-838.
108. Volta U, Bellentani S, Bianchi F B, Brandi G, De Franceschi L, Miglioli L, Granito A, Balli F, Tiribelli C. High prevalence of celiac disease in Italian general population, *Digestive Diseases and Sciences*, 46(7), 2001, 1500-1505.
109. Polanco I, Mearin M L, Larrauri J, Biemond I, Wipkink-Bakker A, Pen A S. Effect of gluten supplementation in healthy siblings of children with celiac disease, *Gastroenterology*, 92(3), 1987, 678-681.
110. Caputo M, Brizzolara R, Schiavo M, Salmaso C, Pesce G, Bagnasco M. Occurrence of overt celiac disease in the elderly following total thyroidectomy, *Journal of Endocrinological Investigation*, 29(9), 2006, 831-833.
111. Roshan B, Leffler D A, Jamma S, Dennis M, Sheth S, Falchuk K, Najarian R, Goldsmith J, Tariq S, Schuppan D, Kelly C P. The incidence and clinical spectrum of refractory celiac disease in a North American referral center, *Official Journal of the American College of Gastroenterology, ACG*, 106(5), 2011, 923-928.
112. Van De Water J M, Cillessen S A, Visser O J, Verbeek W H, Meijer C J, Mulder C J. Enteropathy associated T-cell lymphoma and its precursor lesions, *Best Practice and Research Clinical Gastroenterology*, 24(1), 2010, 43-56.
113. Walker M M, Murray J A. An update in the diagnosis of coeliac disease, *Histopathology*, 59(2), 2011, 166-179.

114. Rubio-Tapia A, Murray J A. Classification and management of refractory coeliac disease, *Gut*, 59(4), 2010, 547-557.
115. Ho-Yen C, Chang F, Van Der Walt J, Mitchell T, Ciclitira P. Recent advances in refractory coeliac disease: A review, *Histopathology*, 54(7), 2009, 783-795.
116. Rubio–Tapia A, Kelly D G, Lahr B D, Dogan A, Wu T T, Murray J A. Clinical staging and survival in refractory celiac disease: A single center experience, *Gastroenterology*, 136(1), 2009, 99-107.
117. Malamut G, Afchain P, Verkarre V, Lecomte T, Amiot A, Damotte D, Bouhnik Y, Colombel J F, Delchier J C, Allez M, Cosnes J. Presentation and long-term follow-up of refractory celiac disease: Comparison of type I with type II, *Gastroenterology*, 136(1), 2009, 81-90.
118. Verbeek W H, Schreurs M W, Mulder C J. Flow cytometric determination of aberrant intra-epithelial lymphocytes predicts T-cell lymphoma development more accurately than T-cell clonality analysis in refractory celiac disease, *Clini Immu*, 126(1), 2008, 48-56.
119. Al-Toma A, Mulder C J. Update on the management of refractory coeliac disease, *Journal of Gastrointestinal and Liver Diseases: JGLD*, 16(1), 2007, 57-63.
120. Johnston S D, Middleton D, McMillan S A, Maxwell P, Hamilton P, Love A G. Genetic, morphometric and immunohistochemical markers of latent coeliac disease, *European Journal of Gastroenterology and Hepatology*, 11(11), 1999, 1283-1288.
121. Meloni G F, Dessole S, Vargiu N, Tomasi P A, Musumeci S. The prevalence of coeliac disease in infertility, *Human Reproduction*, 14(11), 1999, 2759-2761.
122. James S P. National Institutes of Health consensus development conference statement on celiac disease, *Gastroenterology*, 128(4), 2005, S1-9.
123. Di Sabatino A, Corazza G R. Coeliac disease, *The Lancet*, 373(9673), 2009, 1480-1493.
124. Holtmeier W, Caspary W F. Celiac disease, *Orphanet Journal of Rare Diseases*, 1(1), 2006, 1-8.
125. Rubio-Tapia A, Hill I D, Kelly C P, Calderwood A H, Murray J A. American College of Gastroenterology clinical guideline: Diagnosis and management of celiac disease, *The American Journal of Gastroenterology*, 108(5), 2013, 656-676.
126. Review team, Julio C. Bai, Peter Green, Javier Gutierrez-Achury, Michael Schultz, Elena Verdu, Kassem Barada, Thierry Coton, Govind Makharia, Anton LeMair. Celiac disease, *World Gastroenterology Organisation Global Guidelines, J Clin Gastroenterol*, 47(2), 2013, 1-6.
127. Rashtak S, Murray J A. Coeliac disease, new approaches to therapy, *Alimentary Pharmacology and Therapeutics*, 35(7), 2012, 768-781.
128. Lindfors K, Lahdeaho M L, Kalliokoski S, Kurppa K, Collin P, Maki M, Kaukinen K. Future treatment strategies for celiac disease, *Expert Opinion on Therapeutic Targets*, 16(7), 2012, 665-675.
129. Sharma P, McCarty T R, Lange A, Ngu J N, Njei B. Impact of bariatric surgery on outcomes of patients with celiac disease: A nationwide inpatient sample analysis, *Annals of Gastroenterology*, 32(1), 2019, 73-80.
130. Caio G, Volta U, Sapone A, Leffler D A, De Giorgio R, Catassi C, Fasano A. Celiac disease: a comprehensive current review, *BMC Medicine*, 17(1), 2019, 1-20.

Please cite this article in press as: Karra Geetha *et al*. A review on celiac disease, *Asian Journal of Research in Chemistry and Pharmaceutical Sciences*, 12(2), 2024, 43-55.