الجمهورية الجزائرية الديمقراطية الشعبية

People's Democratic Republic of Algeria

وزارة التعليم العالي والبحث العلمي

Ministry of Higher Education and Scientific Research

جامعة 8 ماي 1945

University 8 Mai 1945 Guelma

Faculty of Natural and Life Sciences, Earth and Universe Sciences

Dissertation for the Obtainment of a Master's Degree

Domain: Natural and Life Sciences

Field: Biological Sciences

Specialty/Option: Applied biochemistry

Department: Biology

Theme

Understanding coeliac disease in Guelma: A cross sectional study assessment of prevalence, risk factors and management

Presented by:

-Aggoune Zeineb

-Djelailia Ines

In front of the jury composed of:

- President : Dr. Aissani F	**University of Guelma**
- Examiner : Dr. Doghmane A	**University of Guelma**
- Supervisor: Dr. Yakhlef M	**University of Guelma**

June 2025

Acknowledgment

In the name of Allah, the Most Gracious,
the Most Merciful, all praise and thanks be
to Allah the Almighty, who granted us the strength and

guidance to complete this work.
We extend our sincere gratitude to
the jury members,
Aissani, F. *and* ***Doghmane, A.*** *for their dedication, time, and effort in evaluating our research and providing valuable insights in the field.*

Our deepest appreciation goes to our supervisor, ***Yakhlef M.*** *for her invaluable feedback, unwavering support, and exceptional guidance. Her expertise and dedication have been fundamental to the successful completion of this work.*

Dedication

In the name of Allah, the Most Gracious, the Most Merciful. First and foremost, I offer all praise to Allah, who granted me the strength and perseverance to complete this thesis. It has been a long journey, and I am deeply grateful for the patience He bestowed upon me throughout this process.

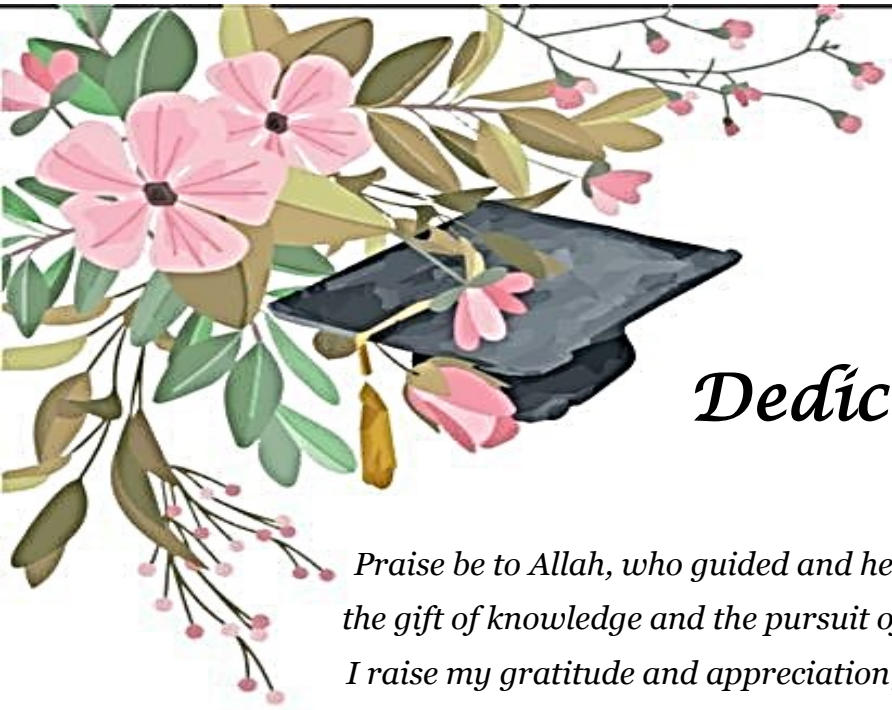
*I extend my deepest gratitude to myself for my ambition and resilience I am truly proud of all that I have achieved. A special tribute goes to my beloved grandmother,**Zakia**, may Allah have mercy on her soul. Her prayers never left me, even in her final moments, and for that, I am eternally thankful.*

*My sincere appreciation also goes to my dear mother,**Saliha**, whose love and prayers have been my unwavering support, and to my father, **Houcine**, whose encouragement has never wavered throughout this journey. To my beloved sister, **Nor El Imane**, for always uplifting me, and to my wonderful siblings **Salsabil**, **Abdel Rahim**, and **Idris** your presence and support mean the world to me.*

*A heartfelt thank you to my dear friend **Shaima**, whose encouragement has been invaluable. I also wish to express my gratitude to my amazing friends **Samah**, **Aroua**, and **Rayan**, who have always stood by my side.*

To each and every one of you, I am deeply grateful for your unwavering support, love, and thout you, this achievement would not have been possible.

Zeineb



Dedication

Praise be to Allah, who guided and helped me, and blessed me with the gift of knowledge and the pursuit of my dreams. To You, O Allah, I raise my gratitude and appreciation for every moment of strength and guidance You granted me on this journey.

*To the dearest people in my life, my mother **Alima**, the source of love and sacrifice, who has been my guiding light and whose prayers accompanied me every step of the way. My father **Lyamin**, my support and strength, who never hesitated to encourage and stand by me. My siblings **Houssam**, **Wael, Moataz**, who gave me strength and smiles in difficult times you were always there for me, and you are part of this success.*

*To **kimou**, thank you for every moment you stood by my side and for your encouragement that gave me the push to continue and move forward.*

This achievement is not mine alone, but belongs to everyone who believed in me and supported me on my journey. Thank you all, and I pray that Allah grants me success in continuing on this path.

Ines

Abstract

The present work is a cross-sectional study conducted in Guelma province over a period of two months (February and March 2025). It aims to assess the prevalence of coeliac disease, the influencing factors, and management strategies. A structured questionnaire was used to collect data on demographic characteristics, dietary habits, and awareness of the disease. The study included 300 participants from diverse age groups and both genders, with data gathered from various locations, including local universities, parks, main streets, and well-known retail stores, providing a comprehensive overview of the disease in the region.

The results indicate that 9.33%(95% CI 6.29 - 13.21) of participants were diagnosed with coeliac disease, with the most affected age group being 9–17 years. Several risk factors were identified, including genetic predisposition (HLA-DQ2/DQ8), nutritional deficiencies, and limited access to gluten-free products. Additionally, modifiable factors such as low awareness of gluten sources and dietary challenges were found to contribute to disease management difficulties.

These findings highlight the importance of early screening and dietary intervention to prevent complications such as osteoporosis, anemia, and intestinal malignancies. Public health strategies should focus on raising awareness, improving access to gluten-free products, and enhancing diagnostic capabilities to support affected individuals.

Keywords: Coeliac disease, prevalence, risk factors, gluten-free diet, cross-sectional study.

Résumé

Le présent travail est une étude transversale menée dans la province de Guelma sur une période de deux mois (février et mars 2025). Il vise à évaluer la prévalence de la maladie cœliaque, les facteurs qui l'influencent et les stratégies de gestion. Un questionnaire structuré a été utilisé pour recueillir des données sur les caractéristiques démographiques, les habitudes alimentaires et la sensibilisation à la maladie. L'étude a impliqué 300 participants de différents groupes d'âge et des deux sexes, avec des données collectées dans divers lieux, notamment les universités locales, les parcs, les rues principales et les magasins bien connus, offrant ainsi un aperçu global de la maladie dans la région.

Les résultats indiquent que 9,33%(95% CI 6.29 - 13.21) des participants ont été diagnostiqués avec la maladie cœliaque, la tranche d'âge la plus touchée étant 9 à 17 ans. Plusieurs facteurs de risque ont été identifiés, notamment la prédisposition génétique (HLA-DQ2/DQ8), les carences nutritionnelles et l'accès limité aux produits sans gluten. En outre, des facteurs modifiables comme la faible connaissance des sources de gluten et les défis alimentaires ont été reconnus comme contribuant aux difficultés de gestion de la maladie.

Ces conclusions soulignent l'importance du dépistage précoce et des interventions alimentaires pour prévenir les complications telles que l'ostéoporose, l'anémie et les cancers intestinaux. Les politiques de santé publique doivent privilégier la sensibilisation, l'amélioration de l'accès aux produits sans gluten et le renforcement des capacités diagnostiques afin de mieux accompagner les individus atteints de cette maladie.

Mots-clés : Maladie cœliaque, prévalence, facteurs de risque, régime sans gluten, étude transversale.

ملخص

يهدف هذا العمل الحالي إلى دراسة مقطعية أجريت في ولاية قالمة على مدار شهرين (فبراير ومارس 2025). يهدف إلى تقييم مدى انتشار مرض السيلياك، والعوامل المؤثرة فيه، واستراتيجيات التعامل معه. تم استخدام استبيان مُنظَّم لجمع البيانات حول الخصائص الديموغرافية، العادات الغذائية، ومدى الوعي بالمرض. شارك في الدراسة 300 فردًا من فئات عمرية متنوعة ومن كلا الجنسين، وتم جمع البيانات من مواقع مختلفة، بما في ذلك الجامعات المحلية، الحدائق، الشوارع الرئيسية، والمتاجر الشهيرة، مما يوفر نظرة شاملة حول المرض في المنطقة.

أظهرت النتائج أن 9.33% (95% CI: 6.29 - 13.21) من المشاركين تم تشخيصهم بمرض السيلياك، وكانت الفئة العمرية الأكثر تأثرًا 9–17 سنة. تم تحديد عدة عوامل خطر، بما في ذلك القابلية الوراثية(HLA-DQ2/DQ8) ، النقص الغذائي، وصعوبة الحصول على المنتجات الخالية من الغلوتين. بالإضافة إلى ذلك، تم رصد عوامل قابلة للتعديل مثل ضعف الوعي بمصادر الغلوتين والتحديات الغذائية التي تؤثر على إدارة المرض.

تؤكد هذه النتائج أهمية الفحص المبكر والتدخل الغذائي لمنع المضاعفات مثل هشاشة العظام، فقر الدم، والأورام المعوية. ينبغي أن تركز استراتيجيات الصحة العامة على زيادة الوعي، تحسين الوصول إلى المنتجات الخالية من الغلوتين، وتعزيز القدرات التشخيصية لدعم المصابين بالمرض.

الكلمات المفتاحية : داء السيلياك، الانتشار، عوامل الخطر، النظام الغذائي الخالي من الغلوتين، دراسة مقطعية.

List of abbreviations

ARA : Anti-Reticulin Antibody

BMD : Bone Mineral Density

BMI : Body Mass Index

CD : Coeliac Disease

DGPA : Deaminated Gliadin Peptide Antibody

EATL : Enteropathy-Associated T-cell Lymphoma

ELISA : Enzyme-Linked Immunosorbent Assay

EMA : Endomysial Antibody

GFD : Gluten-Free Diet

HLA-DQ2 / HLA-DQ8 : Human Leukocyte Antigen DQ2 / DQ8

IBS : Irritable Bowel Syndrome

IEL : Intraepithelial Lymphocyte

IL-15 : Interleukin 15

INF-γ : Interferon Gamma

NCGS : Non-Coeliac Gluten Sensitivity

NK : Natural Killer (cells)

TGA : Transglutaminase Antibodies

tTG : Tissue Transglutaminase

tTGA : Tissue Transglutaminase Antibody

TNF-α : Tumour Necrosis Factor Alpha

List of figures

List of tables

Table of contents

Introduction

Introduction

Coeliac disease (CD) is a chronic autoimmune disorder triggered by gluten, a protein found in wheat, barley, and rye *(Afzal et al., 2024).* It predominantly affects genetically predisposed individuals who express HLA-DQ2 and HLA-DQ8 alleles, which are strongly associated with the disease *(Aboulaghras et al., 2023).* The ingestion of gluten in such individuals initiates an abnormal immune response, causing inflammation of the small intestine. This results in villous atrophy, varying degrees of malabsorption, and the presence of specific antibodies, such as anti-gliadin and anti-tissue transglutaminase *(Tosco et al., 2013)* . Recent research indicates that coeliac disease is a growing global health concern, with an estimated prevalence of 1.4% worldwide *(Singh et al., 2018).* The disease is more common in Europe and Oceania (0.8%), followed by Asia (0.6%), Africa and North America (0.5%), and South America (0.4%). Studies also show that women are more affected than men, with a prevalence of 0.6% in females compared to 0.4% in males *(Caio et al., 2019).* Additionally, the condition is more frequently diagnosed in children (0.9%) than in adults (0.5%), highlighting the importance of early detection and intervention. A recent study on high-risk patients with functional gastrointestinal disorders found a 2.83% prevalence of coeliac disease, with significant associations with age, constipation, and autoimmune disease history *(Syam et al., 2024).*

Diagnosis of coeliac disease involves identifying clinical symptoms, detecting anti-tissue transglutaminase (anti-tTG) antibodies, and confirming intestinal damage through duodenojejunal biopsy, which remains the gold standard *(Caio et al., 2019).* In recent years, non-invasive techniques such as intestinal ultrasound and capsule endoscopy have gained attention for their potential to enhance diagnostic accuracy while minimizing the need for invasive procedures *(Austin et al., 2024).*The cornerstone of treatment remains a lifelong gluten-free diet (GFD), requiring strict avoidance of wheat, barley, and rye *(Verdelho Machado, 2023).* Adherence to this diet alleviates symptoms, reduces antibody levels, and prevents complications like osteoporosis and intestinal malignancies *(Hello et al., 2016).*In recent years, the emergence of gluten-free products has increased public awareness of coeliac disease, yet misconceptions persist regarding the distinction between gluten intolerance and gluten allergy *(Bouteloup, 2016).* While dietary management remains the sole treatment, advancements in pharmacological research, including enzyme therapy and immune-modulating drugs, offer promising potential for future alternatives *(Caio et al., 2019).*

There is no specialised study on coeliac disease in Guelma, Algeria. However, research on coeliac disease and gluten-free diets has been undertaken in other Algerian wilayas, including Tébessa *(Boukezoula et al., 2015).*

The objective of this study was to explore the prevalence, contributing risk factors, and management in the Guelma region. The document is structured in two main sections: the first is a theoretical segment that delves into the definition, mechanisms, and physiological impacts of coeliac disease. The second section concentrates on the practical aspect, detailing a descriptive cross-sectional study carried out through a questionnaire, with an analysis of the results in correlation with various risk factors.

Theoretical part

1) History

The origins of coeliac disease date back to the 2nd century . Aretaeus of Cappadocia, a Greek physician and contemporary of Galen, first described a chronic malabsorption syndrome in children, characterised by persistent diarrhoea, bloating, and progressive wasting. He attributed these symptoms to an intestinal disorder, coining the term “coeliac” from the Greek “koeliakos”, meaning “pertaining to the abdomen” *(Malamut et al., 2009).* Later, in 1888, English physician Samuel Gee offered a comprehensive account of the condition in his influential article "On the Coeliac Affection," published in The St. Bartholomew's Hospital Reports *(Thompson, 2008).* The understanding of coeliac disease took a significant leap forward in 1950 when Dutch paediatrician Willem Karel Dicke demonstrated the connection between the ingestion of cereal products and the onset of symptoms. Dicke identified gluten as the key protein responsible and noted considerable improvement in affected children upon the removal of wheat from their diets *(Kamer et al., 1953).* The autoimmune nature of coeliac disease became evident by the 1970s with the discovery of serum antibodies directed against gluten and endogenous enzymes *(Catroux et al., 2017).* In 1978, Ellis and Linaker reported a case involving a 43-year-old woman who experienced intermittent chronic diarrhoea, peri-umbilical pain, and abdominal distension. Remarkably, her symptoms subsided on a gluten-free diet and reappeared once gluten was reintroduced, even though her jejunal biopsy appeared normal *(Lepers et al., 2004).* Advancements in serological testing and epidemiological research during the 1990s further revealed that coeliac disease was far more common than previously believed, affecting individuals of all ages rather than being confined to childhood *(Catassi et al., 1994; Rostom et al., 2006)*. Up until 2012, gluten intolerance was generally categorised as either coeliac disease or wheat allergy. However, subsequent studies identified a distinct condition known as “gluten sensitivity” or “non-coeliac gluten sensitivity” (NCGS), which is now recognised as the most prevalent form of gluten intolerance *(Molkhou, 2016).*

2) Definition of Coeliac Disease

Coeliac disease is a lifelong autoimmune illness that occurs in the small intestine, which results from ingestion of gluten in genetically predisposed people, predominantly individuals with the HLA-DQ2 or HLA-DQ8 haplotypes *(Aboulaghras et al., 2023).* In diseased patients, ingestion of gluten causes an abnormal immune response, resulting in inflammation and damage to the mucosa of the intestine, characterized by villous atrophy, crypt hyperplasia, and increase in intraepithelial lymphocytes *(Raiteri et al., 2022).*

On the contrary, the usual small intestine is formed of tall finge like villi and organized crypts that are very important for the efficient absorption of nutrients *(Kivelä & Kurppa, 2018)* (figure 1).

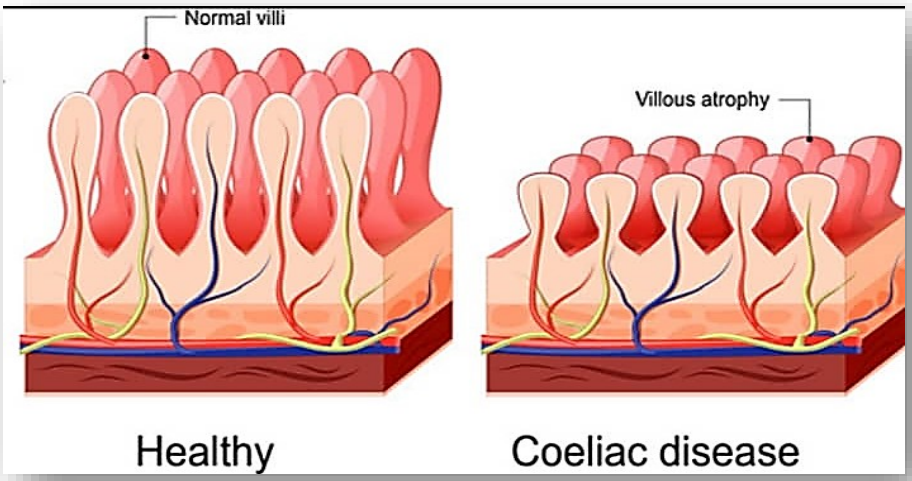


Figure 1: Comparative illustration between normal villi and total villous atrophy *(Kivelä & Kurppa, 2018).*

3) Classification

Among gluten-related disorders, coeliac disease is a well-known autoimmune condition that primarily affects the small intestine. In addition to coeliac disease, there is wheat allergy, which is an allergic reaction to wheat proteins, and non-coeliac gluten sensitivity, where individuals experience symptoms after consuming gluten but without the autoimmune or allergic response seen in other conditions *(Sharma et al.,2020)* (figure 2).

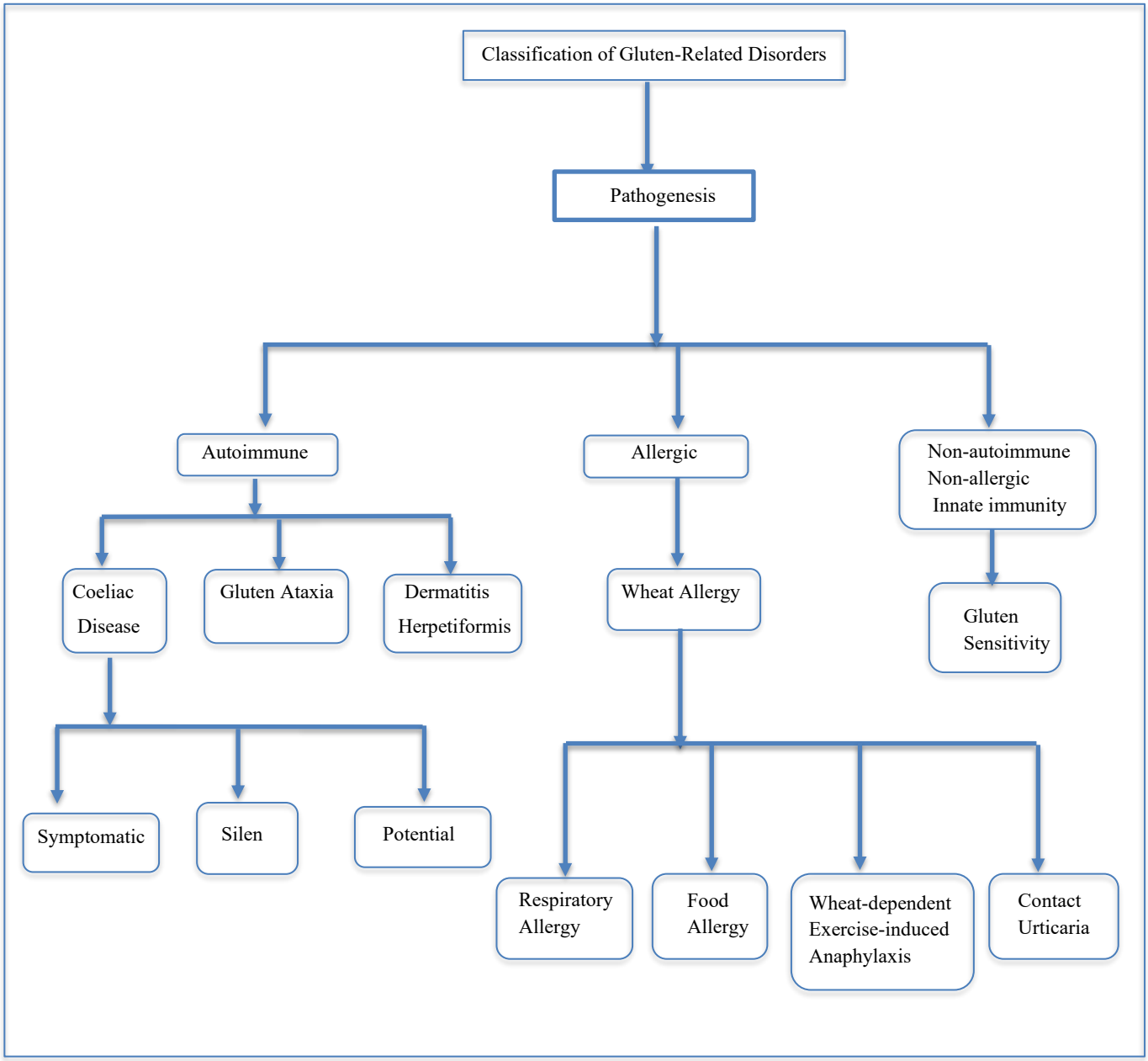


Figure 2: Classification of gluten-related diseases *(Bouteloup, 2016)*

4) Immune mechanisms and pathophysiology

Gluten is the external antigen driving the immunological reaction in coeliac disease. Gluten, consisting of prolamins and glutelins, is typically represented by gliadin in wheat, hordein in barley, and secalin in rye *(Cebolla et al., 2018, Lindfors et al., 2019)*. Upon ingestion, gluten is partially digested by gastrointestinal enzymes, leaving peptides that enter the small intestine's lamina propria. These peptides are deamidated by transglutaminase 2 (TG2), enhancing their binding to HLA DQ2 and DQ8 molecules on antigen-presenting cells

(Lindfors et al., 2019). Presented to CD4+ T cells, these peptides initiate an adaptive immune response, involving TG2-specific B-lymphocytes in Peyer's patches *(Iversen et al., 2020).* Activated T cells secrete cytokines, inducing B cell differentiation into plasma cells that produce antibodies against TG2 and deamidated gliadin peptides *(Catassi et al., 2022).* TGA may increase small bowel permeability and contribute to extraintestinal symptoms *(Lindfors et al., 2019).* Innate immunity also plays a role in coeliac disease development. Stressed enterocytes express interleukin 15 (IL-15) and other cytokines activated by gluten-derived peptides, leading to intraepithelial CD8+ T cell reprogramming and intestinal epithelial cell apoptosis *(Setty et al., 2015, Lindfors et al., 2019).* IL-15 can inhibit regulatory T cells, contributing to the loss of oral tolerance *(van Bergen et al., 2015).*

High proline and glutamine-containing gluten peptides are resistant to enzymatic degradation, and they become immunogenic gliadin peptides. The peptides cross the intestinal epithelium with increased permeability that is normally mediated by release of zonulin and bind immune cells in the lamina propria *(Sallese et al., 2023; Rostami-Nejad et al., 2024).*In the lamina propria, gliadin peptides are deamidated by tissue transglutaminase 2 (TG2), converting glutamine residues into glutamate. This change enhances the binding specificity of gliadin peptides to HLA-DQ2 or HLA-DQ8 molecules on antigen-presenting cells (APCs), which subsequently present the peptides to CD4+ T cells. Stimulation of CD4+ T cells initiates a Th1-predominant immune response, characterized by the secretion of pro-inflammatory cytokines such as interferon γ (INF-γ), IL-21, and tumour necrosis factor α (TNF-α). These cytokines are what cause crypt hyperplasia, villous atrophy, as well as activation of CD8+ T cells, further exacerbating epithelial damage *(Tomer et al., 2023; Rostami-Nejad et al., 2024).*Additionally, innate immunity is implicated, with upregulation of IL-15 triggering natural killer (NK) cells by NKG2D ligands, causing the apoptosis of the epithelial cells (figure 3) *(Rotondi Aufiero et al., 2025).*Moreover, Th2 responses stimulate the differentiation of B cells into plasma cells, which then produce anti-gliadin and anti-TG2 antibodies *(M. du Pré et al., 2020).*

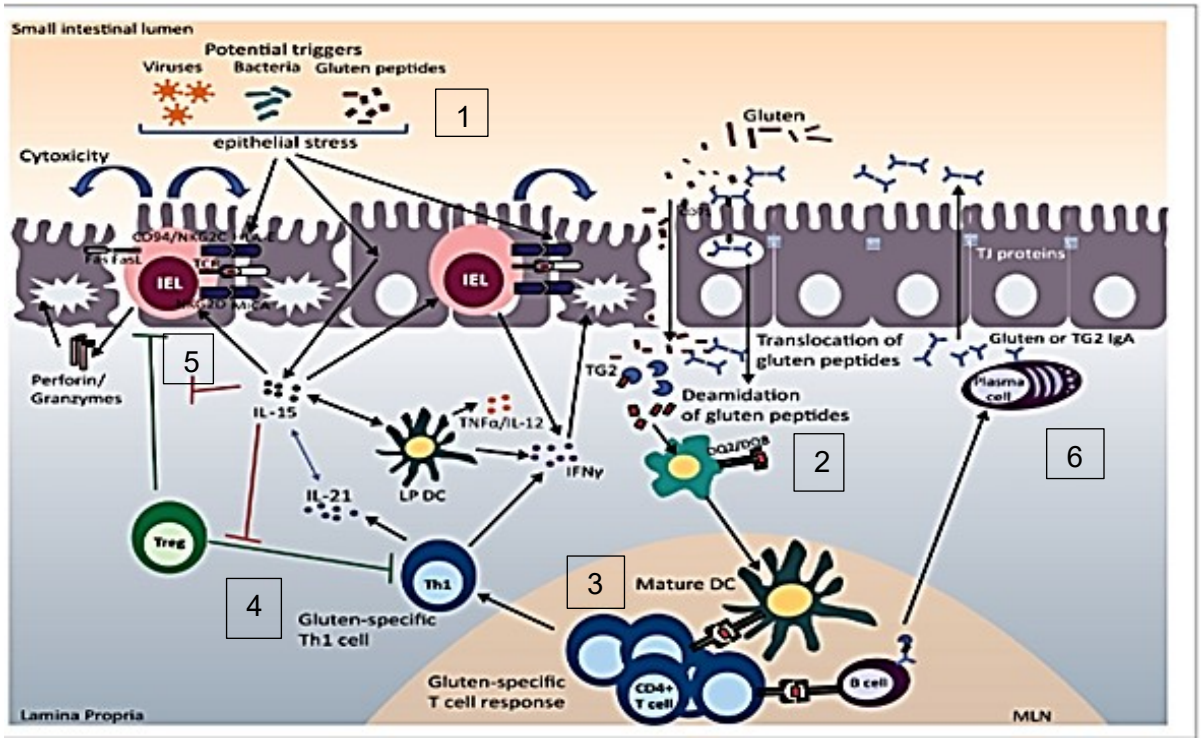


Figure 3: Pathogenetic cascade of coeliac disease (adapted from *Galipeau and Verdu 2014*). Dietary gluten and possibly other additional triggers induce epithelial stress in the intestinal epithelial cells (1). Increased permeability and transcellular transport of gliadin peptides through the epithelium lead to deamidation by TG2 and attachment of gluten peptides to the DQ2/DQ8 molecule (2). APC presents gluten peptide to CD4+ T-cells (3), leading to an agluten-specific T-cell-mediated immune reaction (4). Destruction of the small intestine mucosa is mediated by cytotoxic IELs by activating NK receptors and their ligands. HLA-E and MICA/B (5). This is enhanced by epithelial stress and the secretion of IL-15. Adaptive immune reactions also lead to the differentiation of B-cells to gluten-specific plasma cells. and the secretion of TG2-ab (6). These antibodies may play a role, for example, in the extraintestinal manifestations of coeliac disease. TG2: transglutaminase 2; APC: antigen-presenting cell; DC: dendritic cell; MLN: mesenteric lymph node; PP: Payer's patch; LP: lamina propria; Treg: regulatory T-cell; IL: interleukin; INF: interferon; TNF: tumour necrosis factor; IEL: intraepithelial lymphocyte; TG2-ab: transglutaminase 2 antibodies.

5) Clinical Manifestations of Coeliac Disease

5.1) Gastrointestinal Symptoms

Many of the patients have a variety of gastrointestinal manifestations involving abdominal pain, diarrhoea, constipation, vomiting, and bloating. They present with many mimicking manifestations in other diseases such as gastrointestinal diseases, which involve

irritable bowel syndrome (IBS) that has much greater over-representation of coeliac disease *(Rossi et al., 2024).* Untreated coeliac disease can lead to malabsorption, which results in deficiencies of some nutrients such as iron, vitamin B12, folic acid, and fat-soluble vitamins, which in turn result in systemic symptoms like fatigue and weight loss *(Bianchi et al., 2024).* In addition, even with strict gluten-free diets, these patients may still experience residual gastrointestinal symptoms, suggesting the need for ongoing management and support interventions in order to optimize health outcomes *(Dochat et al., 2024).*

5.2) Extraintestinal Manifestations

Extraintestinal symptoms are also common in coeliac disease, with up to 60% of patients exhibiting one or more such features *(Jericho et al., 2017; Nurminen et al., 2019).*

5.2.1) Anaemia

Anaemia is frequently observed in both paediatric *(Mubarak et al., 2013; Rajalahti et al., 2017)* and adult patients *(Abu Daya et al., 2013; Jericho et al., 2017; Volta et al., 2014),* often resulting from iron deficiency, although vitamin B12 and folic acid deficiencies can also contribute *(Berry et al., 2018; Repo et al., 2017).*

5.2.2) Dermatitis Herpetiformis (DH)

The most well-known dermatological manifestation, DH, is characterised by an intensely pruritic, blistering rash typically located on the elbows, knees, and buttocks. It is seen in about 2% of paediatric and 10–13% of adult patients *(Jericho et al., 2017; Nurminen et al., 2019; West et al., 2014)* and is considered to develop as a complication of long-term untreated coeliac disease *(Salmi et al., 2015).*

5.2.3) Bone Health

Reduced bone mineral density, osteopenia, or osteoporosis is common, with newly diagnosed untreated adults showing prevalence rates as high as 62–72% *(Kurppa et al., 2010a; Vilppula et al., 2011).* Paediatric patients may also have decreased bone density, and growth failure is frequently observed in children *(Nurminen et al., 2019).*

5.2.4) Liver Involvement

Elevated liver enzymes have been reported in both paediatric *(Jericho et al., 2017; Nurminen et al., 2019; Äärelä et al., 2016)* and adult patients *(Castillo et al., 2015; Jericho et al., 2017).* Although these abnormalities often resolve with strict adherence to a gluten-free diet, untreated coeliac disease can, in rare cases, progress to liver failure *(Valvano et al., 2020).*

5.2.5) Joint and Musculoskeletal Symptoms

Joint symptoms, including arthralgia, myalgia, arthritis, and joint effusions similar to those seen in enteropathic arthritis, have been documented in both children and adults *(Jericho et al., 2017; Nurminen et al., 2019).*

5.2.6) Other Manifestations

Additional extraintestinal features include adverse pregnancy outcomes in adults and delayed puberty in children *(Grode et al., 2018a; Jericho et al., 2017),* as well as recurrent aphthous ulcers and dental enamel defects *(Campisi et al., 2007).* Neurological symptoms such as headaches and gluten ataxia have also been reported *(Hadjivassiliou et al., 2010; Jericho et al., 2017),* along with various psychiatric disorders that may be related to gluten ingestion *(Therrien et al., 2020).* Moreover, extraintestinal manifestations may be partly attributed to adaptive anti-gluten immune responses and secondary changes from intestinal damage *(Leffler et al., 2015).* In patients with dermatitis herpetiformis, nearly all exhibit villous atrophy in the small bowel, even if gastrointestinal symptoms are minimal or absent *(Salmi et al., 2014).*

6) Complications of Coeliac Disease

6.1) Malignancies

Coeliac disease can result in several complications if not properly managed. With regard to malignancies, research indicates that the overall cancer risk in both treated and untreated coeliac patients is similar to that of the general population, with some evidence suggesting a reduced risk for cancers such as breast cancer *(Ilus et al., 2014a; Tio et al., 2012).*

However, there is a clearly established elevated risk for certain lymphomas, particularly enteropathy-associated T-cell lymphoma (EATL) and other non-Hodgkin's lymphomas, although improved dietary adherence and milder disease presentations recently may have contributed to a decline in these risks *(Tio et al., 2012; Ilus et al., 2014a).*

In addition, patients with coeliac disease have a three- to fourfold increased risk of developing small-intestinal adenocarcinoma, despite its absolute risk remaining lower than that of non-Hodgkin's lymphoma; there is also some suggestion of an increased risk for colon carcinoma, though findings in this area are inconsistent *(Emilsson et al., 2020; Ilus et al., 2014a; Grainge et al., 2012).*

6.2) Bone Health

Complications also extend to bone health. While a strict gluten-free diet (GFD) can help improve bone mineral density (BMD), individuals diagnosed after achieving peak bone mass may continue to experience osteopenia or osteoporosis even after several years on a GFD, with persistence observed in 9–62% of patients. This is likely due to factors such as impaired

mucosal healing, older age at diagnosis, and nutritional deficiencies related to gluten-free foods, and these patients are almost twice as likely to suffer fractures compared to those without the disease *(Larussa et al., 2017; Pekki et al., 2015; Heikkilä et al., 2015).*

6.3) Pregnancy-Related Complications

Furthermore, untreated coeliac disease has been linked to adverse pregnancy outcomes, including intrauterine growth restriction and preterm delivery. Unrecognised coeliac disease appears to be more prevalent among women with unexplained infertility, although results are not entirely consistent across studies; importantly, women with treated coeliac disease do not seem to experience higher rates of adverse pregnancy outcomes, suggesting that adherence to a GFD may offer some protective effects *(Tersigni et al., 2014; Singh et al., 2016; Celdir et al., 2021; Grode et al., 2018a; Grode et al., 2018b).*

7) Forms of Coeliac Disease Characterized by Marsh Classification

Coeliac disease exists in various forms, each with certain typical clinical and histological features classified by the Marsh classification (figure 4).

7.1) Symptomatic Form

7.1.1) Classic Presentation

This form is typified by extensive damage to the intestine, producing classic features of malabsorption such as chronic diarrhea, bloating, and weight loss. Histologically, it is equivalent to Marsh Stage 3, which is villous atrophy, crypt hyperplasia, and increased intraepithelial lymphocytes (IELs). This results in a reduced absorptive surface and impaired nutrient absorption *(Gruver et al., 2023; Douida et al., 2020).*

7.1.2) Atypical Presentation

This is the most common presentation in adults (>80%) and is typified by non-digestive, mild symptoms such as iron-deficiency anaemia, pubertal retardation, or retardation of growth. These patients typically have Marsh Stages 1 or 2, with crypt hyperplasia and IEL infiltration, but no villous atrophy *(Gruver et al., 2023).*

7.2) Asymptomatic (Silent) Form

There are no overt symptoms of this type of coeliac disease, and it is usually detected on screening in the high-risk patient, such as a family history of coeliac disease. Biopsy results are characteristically Marsh Stage 1 or 2 changes with crypt hyperplasia and IEL infiltration without villous atrophy *(Adams, 2022).*

7.3) Latent Form

Latent type consists of normal mucosa of the bowel (Marsh Stage 0) or minimal IEL invasion (Marsh Stage 1) with no symptoms. Gluten exposure repeatedly results in extension

to symptomatic stages with elevated histological damage *(Gruver et al., 2023; Douida et al., 2020).*

7.4) Refractory Form

This long-standing presentation of coeliac disease is characterized by persistent symptoms and villous atrophy on a strict gluten-free diet for over a year. It is comparable to Marsh Stages 3c (total villous atrophy) or Stage 4 (full mucosal hypoplasia) and is likely to be accompanied by an increased risk of complications such as enteropathy-associated T-cell lymphoma *(Gruver et al., 2023; Douida et al., 2020).*

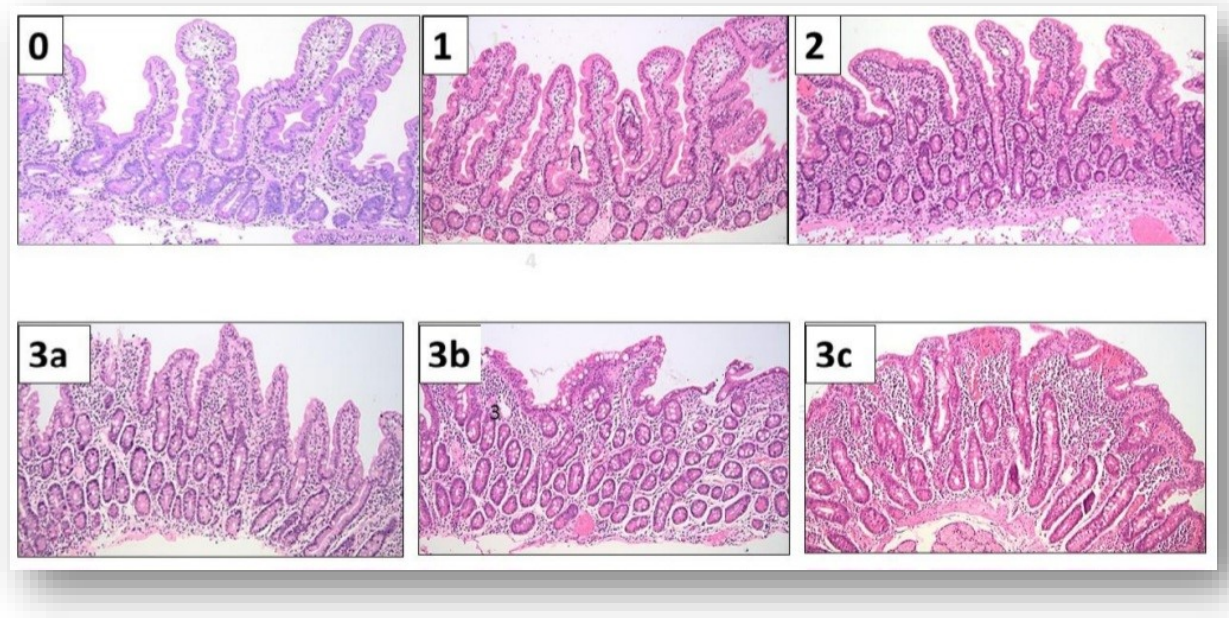


Figure 4: Marsh stages of coeliac disease *(Ian Brown, 2016).*

8) Risk factors

8.1) Gender

Coeliac disease has a higher prevalence among women compared to men, largely due to hormonal, genetic, and clinical reasons. Oestrogen, which is the overweening hormone found among women, stimulates immune system function, which can increase susceptibility to autoimmune disorders like coeliac disease *(Galli et al., 2022).* Additionally, women possess two X chromosomes, so they may double the chance of transmitting susceptibility genes such as TMEM187, which has been established as a cause of coeliac disease *(Hernangomez-Laderas et al., 2023)*. In reality, women are more likely to exhibit non-classical symptoms, such as fatigue and anaemia, and therefore higher rates of diagnosis due to greater healthcare-seeking behavior *(Jansson-Knodell et al., 2018).* Men, although less frequently diagnosed, are likely to report severe presentations such as malnutrition and weight loss, thereby allowing easier and quicker diagnosis *(Jansson-Knodell et al., 2018).*

Men who present with milder or atypical symptoms will go undiagnosed due to reduced healthcare use and lower expression of subtle symptoms *(Galli et al., 2022).* The absence of an additional X chromosome in men reduces their genetic inclination, which partly contributes to the lower incidence compared to women *(Hernangomez-Laderas et al., 2023).*

8.2) Genetic Factors

Coeliac disease has a strong genetic basis, with a prevalence of 3% to 10% among first-degree relatives *(Kurppa et al., 2012a; Singh et al., 2015)* and a high concordance rate of up to 90% in monozygotic twins *(Hervonen et al., 2000; Greco et al., 2002)*. The primary genetic risk factors are HLA-DQ2 and HLA-DQ8, encoded by the HLA-DQA1 and HLA-DQB1 genes *(Sollid 2002)*(Figure5), with over 99.6% of affected individuals carrying one of these haplotypes, particularly HLA-DQ2.5, which presents the highest risk *(Kowalski et al., 2025)*. Homozygous carriers of HLA-DQ2.5 face an increased likelihood of developing the disease due to enhanced immune reactivity to gluten *(Caio et al., 2019).*

Despite this strong genetic predisposition, only 1% of the general population develops coeliac disease, despite 30–40% carrying the associated haplotypes, highlighting the importance of environmental and immunological factors *(Leonard et al., 2017).* Genetic testing is primarily used to rule out coeliac disease rather than confirm it, as the presence of HLA-DQ2/DQ8 alone is not sufficient *(Caio et al., 2019).* Additionally, 57 non-HLA genetic variants across 39 loci contribute to susceptibility, mainly affecting immune responses *(Trynka et al., 2011; Gutierrez-Achury et al., 2015).* The highest risk is observed in individuals homozygous for DQB1*02, with seroprevalence rates reaching 40% in high-risk children by age ten *(Pietzak et al., 2009; Lionetti et al., 2014).* Although HLA-DQ2 and DQ8 are common in 50% of the Western population, only a minority develop coeliac disease, reinforcing the role of additional genetic and environmental influences *(Kårhus et al., 2018; Vriezinga et al., 2014; Liu et al., 2017)*. Non-HLA genetic factors account for about 15% of the genetic risk, and their inclusion in genetic testing can improve risk prediction, particularly in high-risk individuals *(Romanos et al., 2014; Sharp et al., 2020)*. However, current genetic discoveries explain only 50% of the disease's heritability, suggesting additional unidentified factors *(Trynka et al., 2011).*

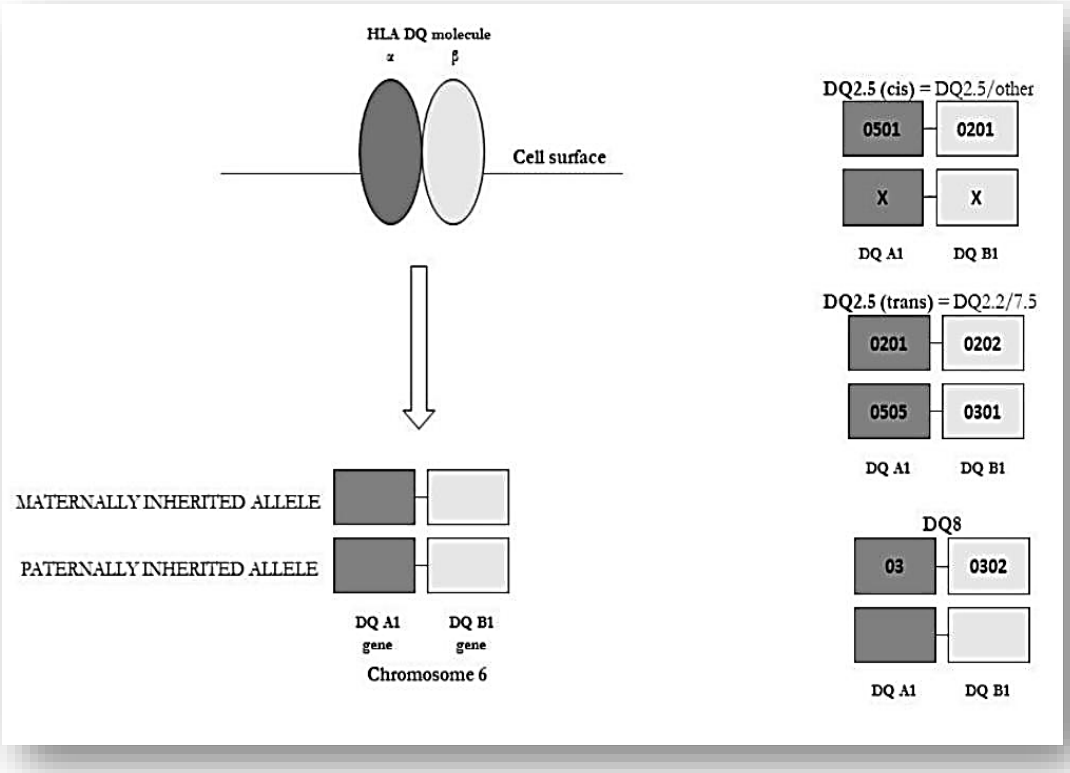


Figure 5: Composition of human leukocyte antigen (HLA) molecule and HLA-DQ2/8 haplotypes.

Adapted from Sollid 2002 and Sollid & Lie 2005.

8.3) Environmental factors

Environmental factors also play a critical role in inducing coeliac disease in those genetically susceptible *(Brown et al., 2018; Lindfors et al., 2020).* In addition to exposure to gluten, additional environmental contributors have been implicated, such as viral infections causing immune tolerance impairment, intestinal microbiota alterations, and early exposure to antibiotics *(Verdu and Schuppan, 2021; Dydensborg Sander et al., 2019).* Variation in coeliac disease prevalence in populations having similar genetic background and comparable gluten consumption suggests that additional, as yet unknown, environmental exposures may play a role *(Catassi et al., 2022).*

8.4) Triggers

The consumption of gluten in genetically predisposed individuals primarily precipitates coeliac disease. However, other factors have been implicated in the precipitation or diagnosis of the disease. These include major physiological or psychological stressors such as pregnancy, major surgery, severe infections, or overwhelming physical or emotional stress. Pregnancy, for instance, can alter immune regulation and endocrine balance, exacerbating the disease. Major

surgery and infections may also increase intestinal permeability, revealing a subclinical state in predisposed subjects. The role of such environmental stressors in the onset of coeliac disease has been stressed by recent studies *(Barone & Auricchio, 2021; Serin et al., 2024).*

8.5) Other Factors

Recently published studies show that several other possible risk factors may affect the development or course of coeliac disease:

8.5.1) Vitamin D Deficiency

Vitamin D deficiency has been considered to be among the co-factors in the development and progression of coeliac disease, given its immunomodulatory role in maintaining intestinal immunity as well as gut barrier integrity *(Infantino et al., 2022).* Dysregulation of these processes may result in increased inflammation and hyperactivity of the immune system, thereby exacerbating intestinal damage in coeliac disease patients *(Infantino et al., 2022).* Research indicates that the children with coeliac disease often have low blood levels of vitamin D, for which the connection to the disease's severity and development is yet unknown *(Sun et al., 2024).*

8.5.2) Gut Microbiome Changes

The gut microbiome, the complex array of microbes inhabiting the intestines, is increasingly well known as an active player in immune system maturation and regulation. Dysbiosis, a disruption of structure and function in the gut microbiota, has been observed in coeliac disease *(Galipeau & Verdu, 2014).* Other variables, such as delivery mode (caesarean section versus vaginal), early antibiotic use, and infant feeding practices, can influence the establishment of the gut microbiome and may potentially be involved in the risk of coeliac disease in genetically susceptible individuals *(Dydensborg Sander et al., 2019).*

8.5.3) Viral Infections

Certain viral infections, particularly enteroviruses, have been suggested as environmental triggers for coeliac disease autoimmunity *(Brown et al., 2018; Lindfors et al., 2020)*. Molecular mimicry, since viral antigens have a similar structure to gluten peptides, might lead to the activation of gluten-reactive T cells following a viral infection *(Lindfors et al., 2020).*

8.5.4) Increase in Intestinal Permeability

Increased intestinal permeability, or leaky gut, has been suggested to play a role in the pathogenesis of celiac disease. With disruption of the intestinal barrier, gluten peptides can traverse the epithelial layer into the lamina propria and activate the immune system with consequent inflammation. These processes are governed by conditions including gut

microbiota, food constituents, and inflammatory mediators. According to research, intestinal permeability plays a critical role in autoimmune illnesses, like celiac disease *(Di Vincenzo et al., 2023).*

9) Diagnostics for Coeliac Disease

9.1) Serological Testing

Serologic tests are essential for diagnosing coeliac disease, monitoring response to a gluten-free diet, and evaluating its prevalence *(Syage et al., 2023; Shatnawei et al., 2023)*. Early tests such as anti-reticulin (ARA) and anti-gliadin antibodies (AGA) have largely been replaced by endomysial antibody (EMA) assays, which offer improved sensitivity and specificity *(Syage et al., 2023).* However, EMA testing is labour-intensive and observer-dependent, leading to the adoption of ELISA-based tests that detect antibodies against tissue transglutaminase (tTG) *(Shatnawei et al., 2023).* The tTG antibody (tTGA) assay is now recommended as the first-line serologic test for coeliac disease *(Syage et al., 2023).* Additionally, deaminated gliadin peptide antibody (DGPA) tests have broadened the diagnostic options, especially in patients with IgA deficiency *(Shatnawei et al., 2023).* Although seronegative coeliac disease is rare, high tTGA titers remain highly specific for the condition *(Syage et al., 2023).*

9.2) Small Bowel Biopsy

Small bowel biopsy has been considered the gold standard for the diagnosis of coeliac disease because it exposes significant histological abnormalities such as villous atrophy, crypt hyperplasia, and increased intraepithelial lymphocytes *(Kowsari et al., 2019).* Biopsy should be undertaken with the patient remaining on gluten for proper diagnosis *(Wei et al., 2019).* The severity of mucosal damage is graded based on Marsh classification, with modifications by Oberhuber providing a better discrimination between stages of disease *(Sali et al., 2019).* Histological examination also includes villus height-to-crypt depth and intraepithelial lymphocyte count, which are important indices of severity of disease *(Kowsari et al., 2019).* While serological assays such as tissue transglutaminase (tTG) IgA can be useful in diagnosis, they are not always diagnostic, especially with selective IgA deficiency *(Wei et al., 2019).*

9.3) Differential Diagnosis

Differential diagnosis is crucial because other conditions may present with villous atrophy and crypt hyperplasia *(DeGaetani et al., 2013; Rubio-Tapia et al., 2013).* Conditions such as tropical sprue typically occur in individuals from tropical regions and present with malabsorption *(DeGaetani et al., 2013).* Autoimmune enteropathy usually manifests as refractory diarrhoea in adults *(Rubio-Tapia et al., 2013).* Inflammatory bowel disease (IBD), particularly Crohn's disease, may also show similar histologic changes *(DeGaetani et al., 2013;*

Rubio-Tapia et al., 2013). A thorough clinical evaluation including patient history, serologic testing, imaging, and additional laboratory studies is necessary to distinguish between these conditions and avoid misdiagnosis *(DeGaetani et al., 2013; Rubio-Tapia et al., 2013).*

9.4) Screening

For screening purposes, the IgA-tTGA assay is preferred due to its high sensitivity and specificity *(Lebwohl et al., 2018; Lindfors et al., 2019).* Screening strategies include active case-finding among individuals with symptoms suggestive of coeliac disease and testing of at-risk groups, such as first-degree relatives or those with other autoimmune conditions *(Kivelä and Kurppa, 2018; Lindfors et al., 2019)*. Although coeliac disease meets WHO criteria for mass screening, further research is needed to assess the cost-effectiveness and potential psychosocial impacts on asymptomatic individuals and to determine the optimal screening protocols *(Kivelä and Kurppa, 2018; Lindfors et al., 2019).*

10) Treatment and Follow-Up of Coeliac Disease

The only proven treatment for coeliac disease is a lifelong gluten-free diet (GFD), which involves strictly avoiding wheat, barley, and rye *(Bascuñan et al., 2017).* Most patients see improvement in symptoms within days to weeks, although full intestinal healing may take years—30–40% of adults still show villous atrophy one year after starting the GFD, while children recover faster *(Pekki et al., 2015).*

Maintaining a GFD can be challenging due to social, economic, and labelling issues, with adherence rates reported between 42% and 96% *(Kivelä et al., 2022; See et al., 2015).* Healthcare providers should also check medications for potential gluten content to ensure the safety of patients with celiac disease *(Silvester et al., 2016).* For patients who do not respond adequately to a GFD or find the diet too burdensome, novel therapies are under investigation. These include the anti-IL-15 monoclonal antibody AMG 714, larazotide (which reduces gut permeability), glutenase ALV003, and the transglutaminase inhibitor ZED1227 *(Kivelä et al., 2021; Schuppan et al., 2021).*

Regular follow-up is vital to monitor dietary adherence, symptom improvement, and mucosal healing, as well as to address nutritional deficiencies and social or economic challenges *(Al-Toma et al., 2019; Ludvigsson et al., 2014).*

11) Epidemiology

Advances in diagnostic methods and epidemiological research have transformed our understanding of coeliac disease from a rare disorder into a significant global public health issue *(Naiyana Gujral et al., 2012).*

Recent studies indicate that coeliac disease is more prevalent than previously estimated. Globally, the prevalence ranges between 0.5% and 1%, with significant regional variations *(Al Kindi et al., 2023)*. In Europe, Germany reports a low prevalence of 0.2%, while Finland records one of the highest rates at 2–3% *(Makharia et al., 2022).*

In Algeria, the prevalence has increased significantly, with recent studies estimating it at 1.43% *(Abed et al., 2023).* A study in Sidi Bel Abbes reported a decline in incidence from 12.9 per 100,000 person-years in 2015 to 8.5 per 100,000 in 2020 *(Asma et al., 2023).* Additionally, research from Eastern Algeria highlights differences in symptoms and diagnosis between children and adults, reinforcing the need for improved screening programs *(Mehadji et al., 2023).*

Globally, the highest prevalence rates have been observed in Western Sahara (5.6%), Mexico (1.5–3.5%), and Finland (2–3%) *(Gujral et al., 2012).* Studies also indicate that the prevalence of coeliac disease in developing countries is rising due to dietary changes and increased consumption of processed gluten-containing foods*(Lionetti & Catassi, 2011).*

Overall, the growing body of epidemiological evidence has reshaped our view of coeliac disease, establishing it as a common lifelong disorder that poses a significant public health challenge worldwide *(Catassi & Fasano, 2012).*

Practical part

Materials and Methods

1) Study Objectives

The aim of this study was to examine the prevalence of coeliac disease among residents of Guelma province within a specific timeframe. The research sought to determine the percentage of individuals diagnosed with coeliac disease at the time of data collection while also evaluating the main contributing factors, the diagnosis methods, follow-up, and management of the illness.

2) Description of the Study and Participants

This descriptive, cross-sectional study was conducted in Guelma province over a period of two months (February and March 2025). Using questionnaires, data was collected from a total of 300 participants, representing diverse age groups and both genders. Data was gathered from various locations, including the faculties of the university of Guelma, parks, main streets, and well-known retail stores. The participants were chosen randomly without any prior emphasis on their medical history. Individuals identified as having coeliac disease were coincidental inclusions during the data collection process.

3) Minimum sample size determination

The sample size for this study was determined using a sample size calculator https://www.calculator.net/sample-size-calculator.html,considering a 95% confidence level , a 2% margin of error , and 2% population proportion .

Based on this, the minimum required sample size was 189 participants. However, as the expected response rate was 60%.

To ensure the collection of sufficient responses,315 questionnaires were distributed. This adjustment accounted for the anticipated non-response rate, ensuring the validity and reliability of the collected data.

4) Data Collection

Data were gathered through the distribution of a structured questionnaire to 315 participants (Appendix1). The questionnaire was drafted in Arabic to ensure clarity and accessibility for individuals from all educational backgrounds. During distribution, support was offered to participants who required assistance in completing the form.

The questionnaire was organized into five sections, covering the following topics:

Section 1: General Information

This section aimed to gather basic demographic data, including:

- Height and weight

- Age
- Gender
- Educational level
- Place of residence

Section 2: Knowledge About the Disease

Focused on evaluating participants' awareness and understanding of celiac disease:

- Definition of gluten sensitivity
- Knowledge about gluten and its sources in food

Section 3: Information About the Disease

Designed to collect specific medical data:

- Presence of gluten sensitivity
- Age at the onset of symptoms
- Key symptoms experienced
- Diagnostic methods used
- Associated diseases
- Family medical history

Section 4: Diet and Daily Life

Explored lifestyle adaptations to living with celiac disease:

- Adherence to a gluten-free diet
- Challenges encountered
- Types of gluten-free products consumed
- Difficulties faced when eating out

Section 5: Improving Awareness and Education

This section targeted ways to enhance knowledge and understanding of the disease:

- Need for awareness campaigns
- Preferred methods for spreading knowledge (e.g., media, health campaigns, educational sessions)

5) Statistical Analysis

Descriptive statistical analysis was carried out using Microsoft Excel 2016. This included the computation of means, standard deviations, and percentages, as well as the generation of graphical representations. Quantitative data are reported as mean ± standard deviation (SD).

Results and discussion

1) General aspect of the results

The study was conducted by distributing 315 questionnaires , with only 300 completed responses received, reflecting a response rate of 95.2%.

1.1) Gender

Our sample consisted of 300 individuals, with a predominance of females, who accounted for 60.33% (181 cases), while males represented 39.67% (119 cases). This corresponds to a female-to-male sex ratio of approximately 1.52 (Figure 6).

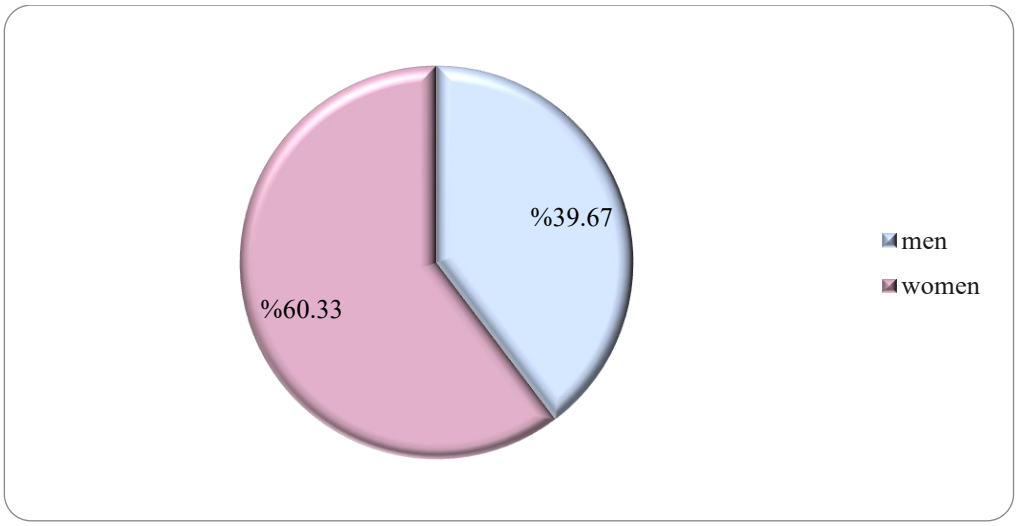


Figure 6: Distribution of the Participants by gender

1.2) Age

A total of 300 individuals participated in this study, with ages ranging from 9 to 68 years. They were categorized into six age groups (Table 1). The highest proportion of participants was recorded in the [19–28] age group, representing 42.33% of the total sample . This was followed by the [29–38] group with 24.67% , and the [39–48] group with 13.33%. The [9–18] age group accounted for 9.67%, while the lowest proportions were observed in the [49–58] and [59–68] age groups, representing 6.67% and 3.33%, respectively.

The average age of the participants was 29.13 ± 12.47 years.

Table 1: Distribution of participants by age

Age group	[9-18]	[19-28]	[29-38]	[39-48]	[49-58]	[59-68]
Effective	29	127	74	40	20	10
Percentage (%)	9.67%	42.33%	24.67%	13.33%	6.67%	3.33%

1.3) BMI (Body Mass Index)

Figure 7 presents the distribution of the participants based on their Body Mass Index (BMI). The majority, 44%, fall within the normal weight range ($18.5 \leq BMI < 25$). Overweight individuals make up 30% of the group ($25 \leq BMI < 30$)., while 14.67% are categorized as obese, having a BMI above 30 ($BMI \geq 30$). On the other hand, 11.33% of the participants are considered underweight ($BMI < 18$).

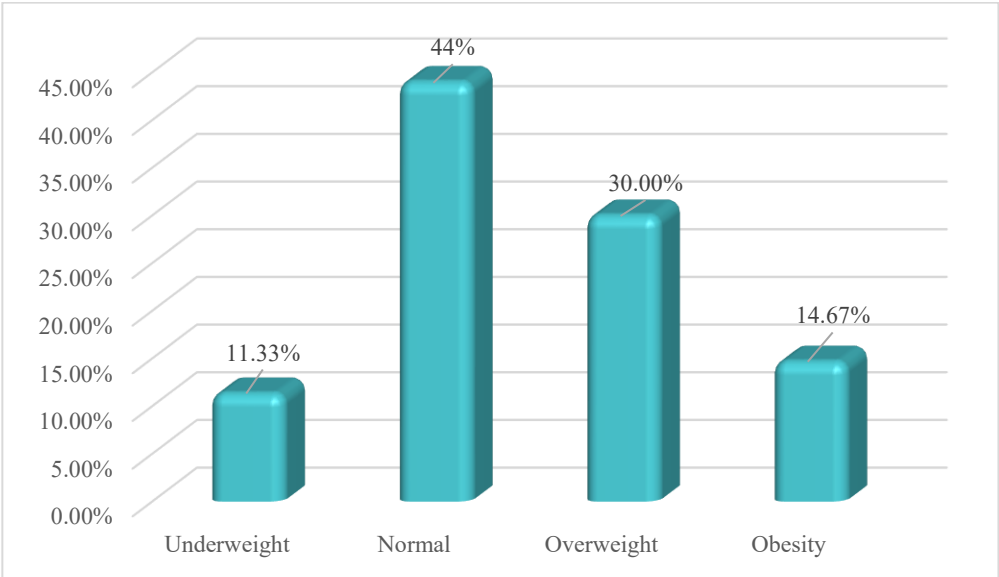


Figure 7: Distribution of participants according to the BMI

1.4) Residence

The distribution of participants according to their place of residence shows that the majority (58%) live in Guelma city (urban areas), while 42% reside in rural regions, as shown in Figure 8.

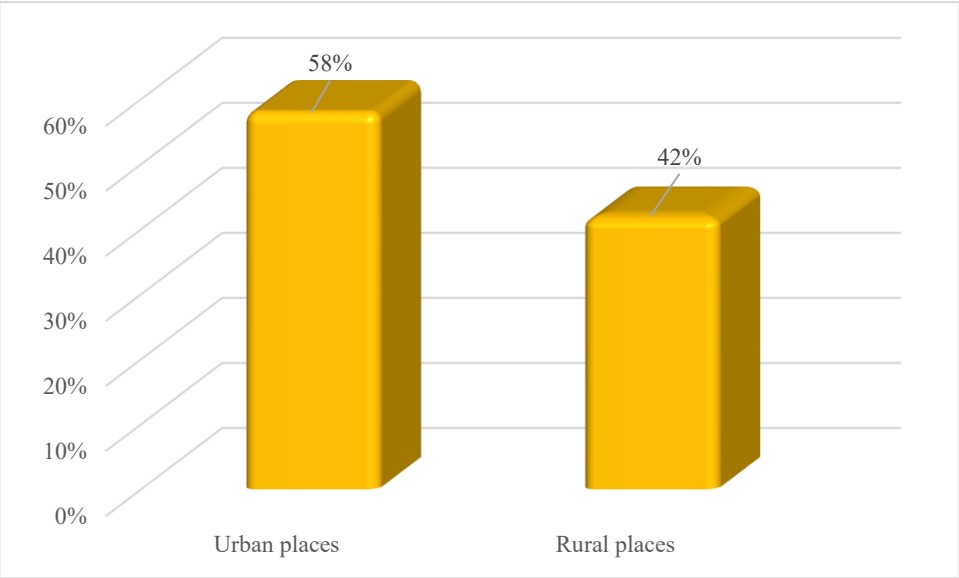


Figure 8: Distribution of Participants by Residential Area

1.5) Prevalence of coeliac disease

According to our findings, the prevalence of coeliac disease among the studied population is 9.33% (95% CI 6.29 - 13.21) , while the remaining 90.67% did not show signs of the disease and were considered healthy (Figure 9).

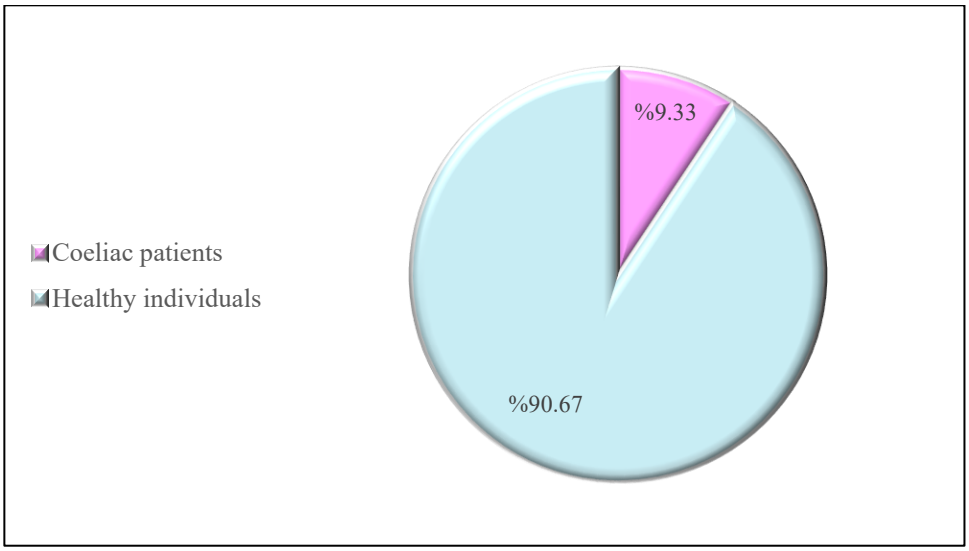


Figure 9: Distribution of Participants According to Coeliac Disease Status

2) Description of patients with coeliac disease

2.1) Gender

Based on the gender distribution, the prevalence among females was 12.71%, while 87.29% remained unaffected. Among males, 95.80% were unaffected, whereas 4.20% were affected,. This corresponds to a female-to-male sex ratio of 4.6 (figure 10).

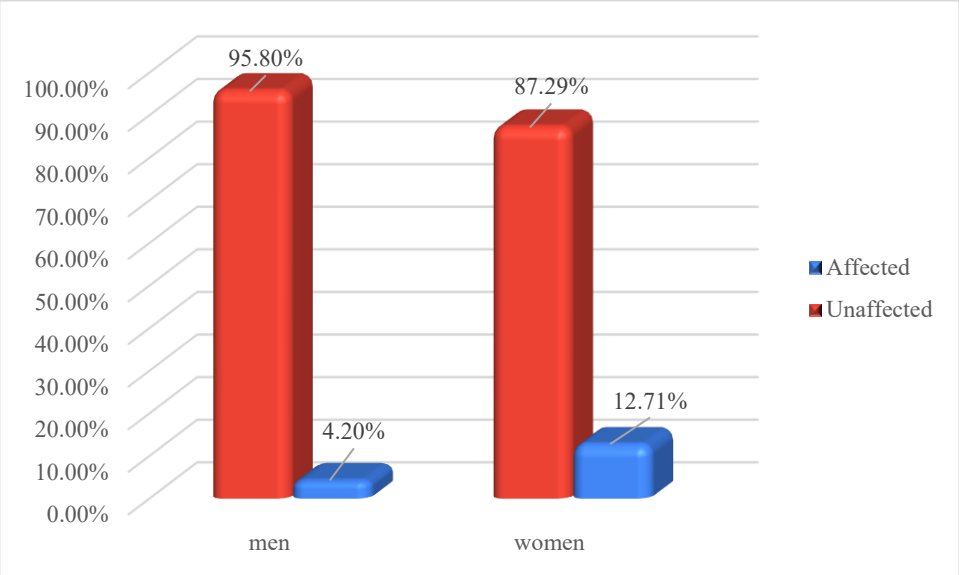


Figure 10: Gender Distribution of the Patients

2.2) Age

The age of the 28 patients included in this study ranged from 9 to 53 years. Participants were grouped into five age categories (Table 2). The age groups [9–17] and [18–26] each represented 28.57% of the total sample . The highest proportion was recorded in the [27–35] age group, comprising 32.14%. The lowest proportions were recorded in the [36–51] and [45–53] age groups, accounting for 7.14% and 3.57%, respectively.

The average age of the participants was 24.36 ± 10.37 years.

Table 2: Distribution of coeliac disease patients by age

Age group	[9-17]	[18-26]	[27-35]	[36-44]	[45-53]
Effective	8	8	9	2	1
Percentage %	28.57%	28.57%	32.14%	7.14%	3.57%

2.3) Description of patients with coeliac disease according to the BMI

The patients with coeliac disease were divided into four categories based on BMI (figure11). The largest proportion, 53.57% (15 cases), had a normal BMI ($18.5 \leq BMI < 25$). Underweight patients ($BMI < 18$) accounted for 21.43% (6 cases), while 21.43% (6 cases) were classified as overweight ($25 \leq BMI < 30$). Only one patient, representing 3.57% of the sample, was categorized in the first-degree obesity group ($BMI \geq 30$).

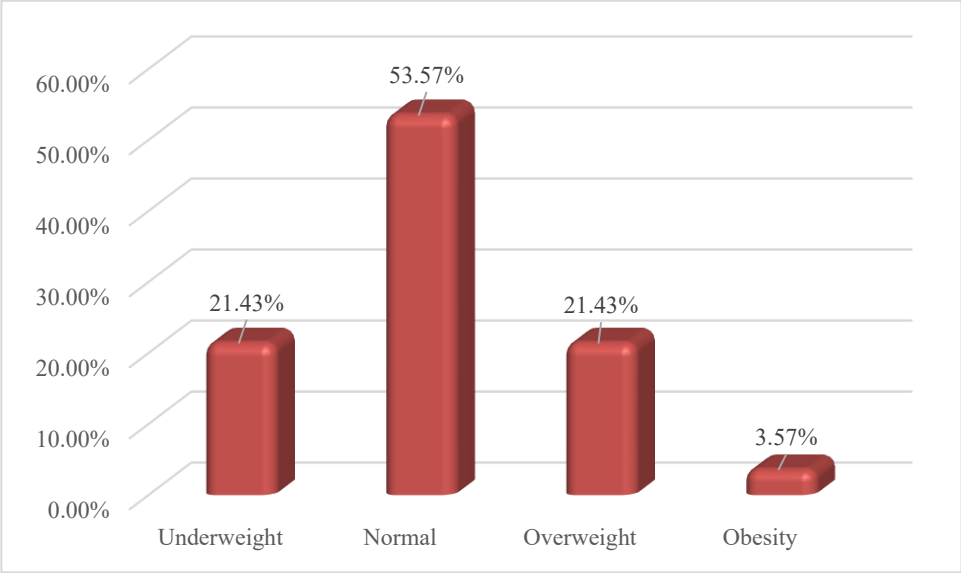


Figure 11: Distribution of patients with celiac disease according to BMI

2.4) Regional Distribution of Coeliac Disease Cases

This study examined coeliac disease cases among participants from Guelma city (urban areas) and its neighboring rural municipalities. Results showed that 78.57% of those diagnosed with coeliac disease lived in urban areas, whereas only 21.42% were from rural locations (Table3).

Table 3: Percentage of Coeliac Disease Cases Across Urban and Rural Areas

Residence	Rural areas	Urban areas
Effective	6	22
Percentage %	21.42%	78.57%

2.5) Diagnosis

The distribution of diagnosis locations among the surveyed patients shows variations in where they were identified(figure12). The largest proportion (71.43%) of cases were diagnosed at a gastroenterologist's clinic (20 individuals), while a smaller percentage (17.86%)received their diagnosis at a general practitioners' clinic(5 individuals). The lowest proportion (10.71%) of cases were diagnosed in a hospital or medical center(3 individuals).

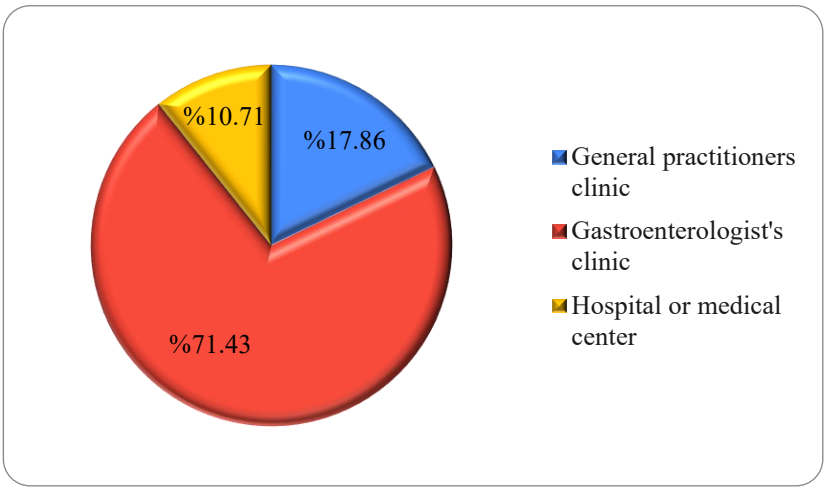


Figure 12: Distribution of Diagnosis Locations Among Patients

The diagnostic methods used among patients showed varying proportions (Figure 13). Intestinal biopsy was the most commonly used method, accounting for 53.57% of cases. This was followed by blood tests at 25%. In 21.43% of cases, diagnosis was made based solely on the presence of clinical symptoms.

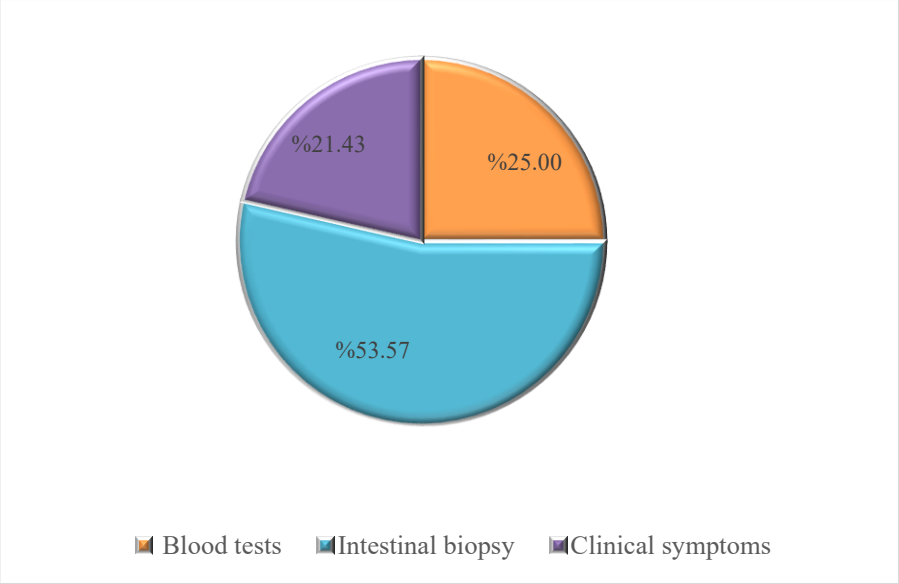


Figure 13: Relative Distribution of Diagnostic Techniques Among Coeliac Disease Patients

2.6) Age of Disease Onset

The age at disease onset among the surveyed individuals ranges between 1 and 30 years, with an average age of 11.39 ± 7.93 years. The distribution indicates that 53.57% of cases emerged between 1 and 10 years, while 25% of patients experienced disease onset between 11 and 20 years. Finally, 21.43% of cases were recorded in the 21 to 30 year range (Figure 14).

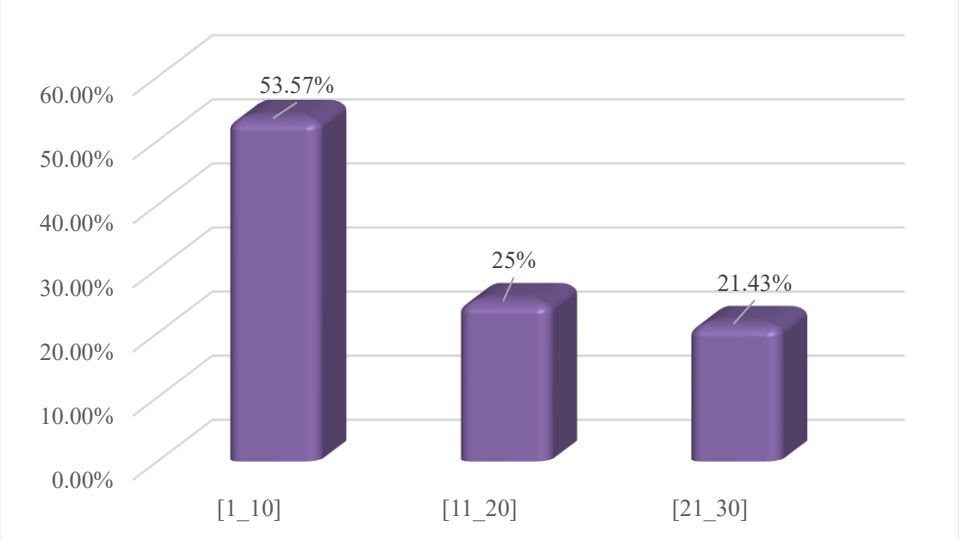


Figure 14: Distribution of patients based on the age of disease onset

2.7) Clinical Manifestations of Coeliac Disease

An analysis of symptoms among the surveyed patients shows that 100% experienced digestive issues, including bloating, diarrhea, and constipation. Additionally, 21.43% reported weight loss, while 28.57% suffered from persistent fatigue and exhaustion.

Abdominal pain was noted in 14.29% of cases, whereas skin problems, such as rashes, were observed in 17.86%. Furthermore, hair loss was identified in 10.71%, along with other symptoms (Figure 15).

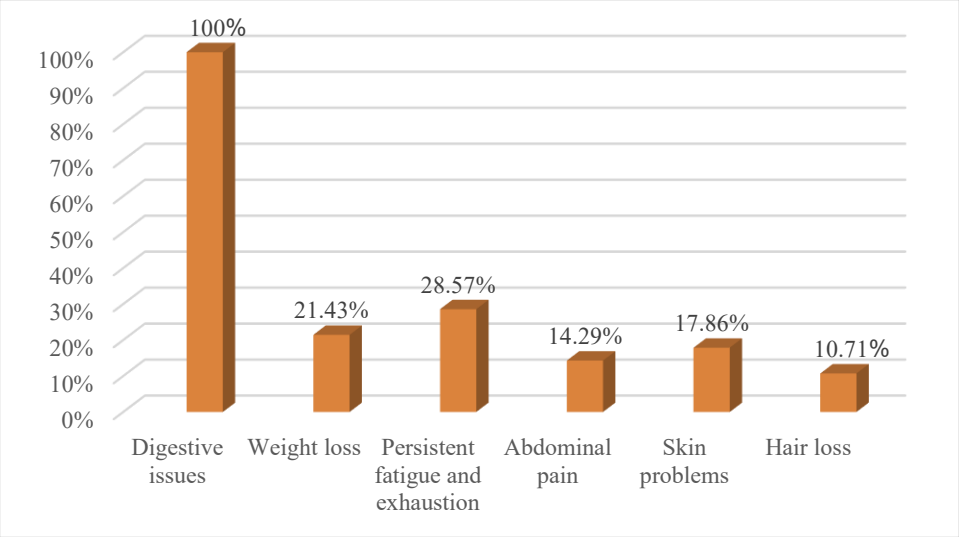


Figure 15: Distribution of Symptoms Among Patients

2.8) Family history of coeliac disease

As shown in figure 16, 21.43% of the participants answered "yes" to having a family history of celiac disease. In contrast, 78.57% responded "No," indicating no known cases of the disease among their family members.

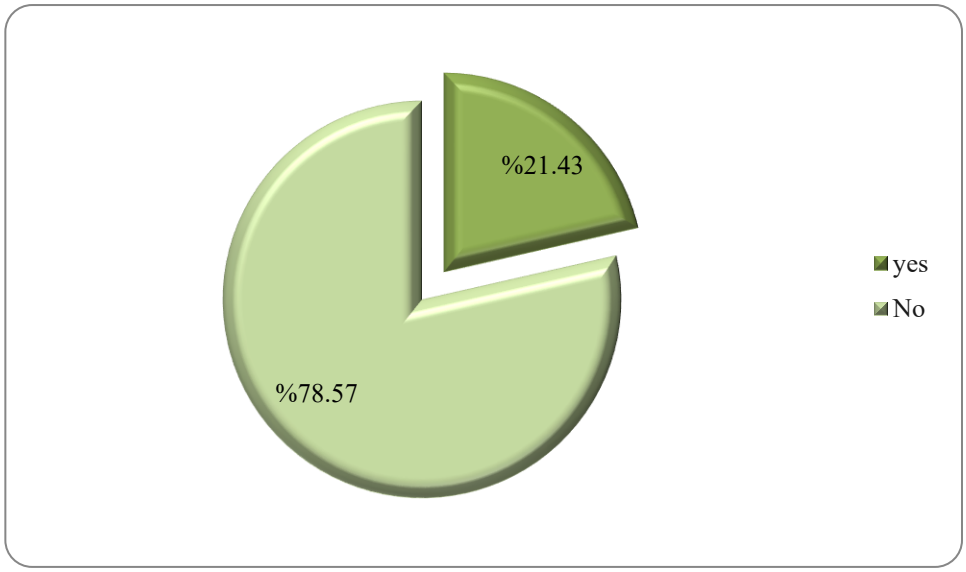


Figure 16: Distribution of participants according to the presence or absence of a family history of coeliac disease.

According to the results shown in figure 17, sisters were the most frequently reported family members affected by celiac disease, representing 50% of the participants. Maternal cousins came next with 33.33%, while brothers were the least affected, reported by only 16.67% of the participants.

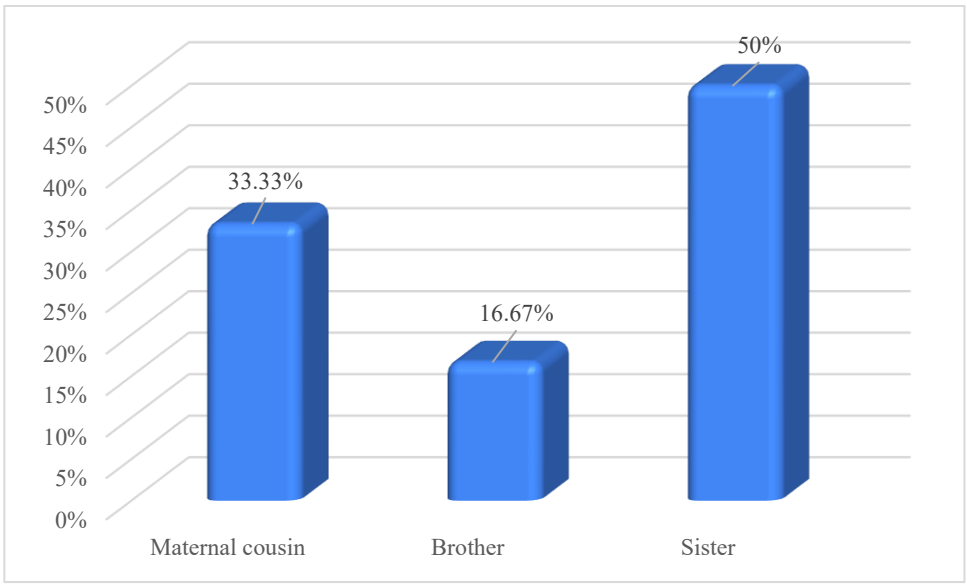


Figure 17: Distribution of participants based on which family members are affected by coeliac disease.

2.9) Associated Pathologies in Coeliac Patients

The analysis of the collected data revealed that 39.29% of the participants reported having some health issues, whereas the majority, 60.71%, stated that they do not suffer from any illnesses (Figure 18).

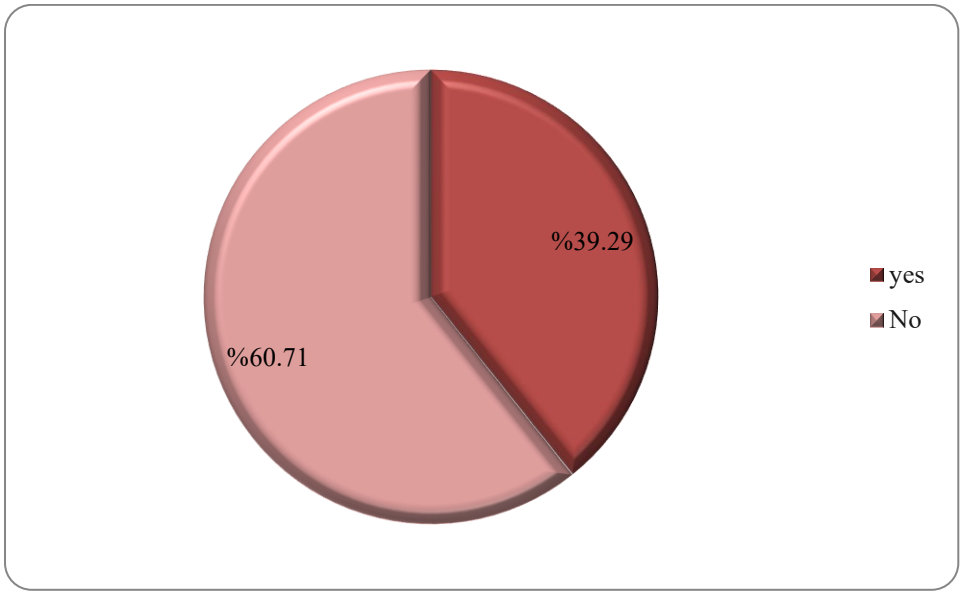


Figure 18: Distribution of Other Diseases Associated with Coeliac Patients

According to our results, anemia is the most prevalent condition among coeliac disease patients, with a rate of 81.82%. Meanwhile, diabetes follows at 18.18% (figure 19).

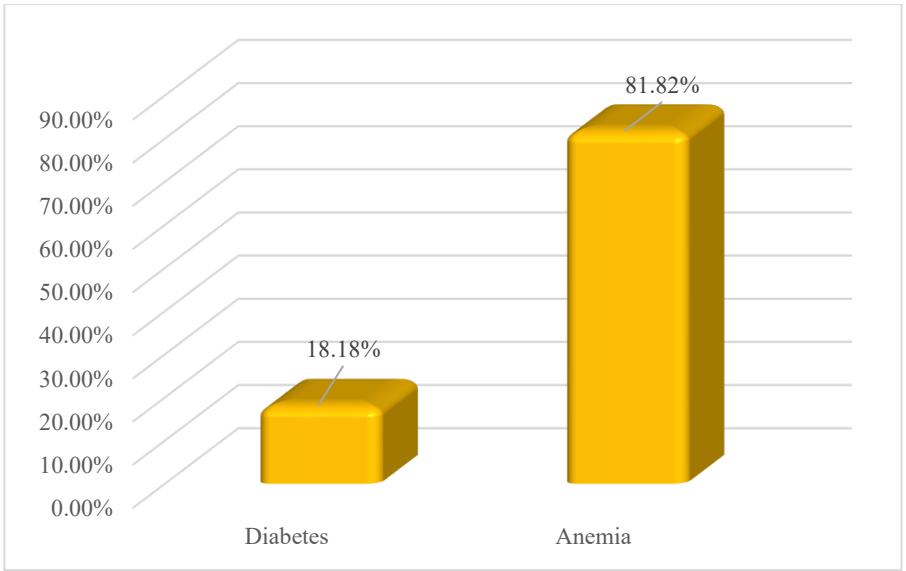


Figure 19: Distribution of Associated Diseases Among Patients.

2.10) Coeliac disease management

Our findings indicate that non-compliance is the most common dietary pattern among participants, accounting for 42.86%. This is followed by occasional gluten consumption at 35.71% and strict adherence to a gluten-free diet at 21.43%(figure 20).

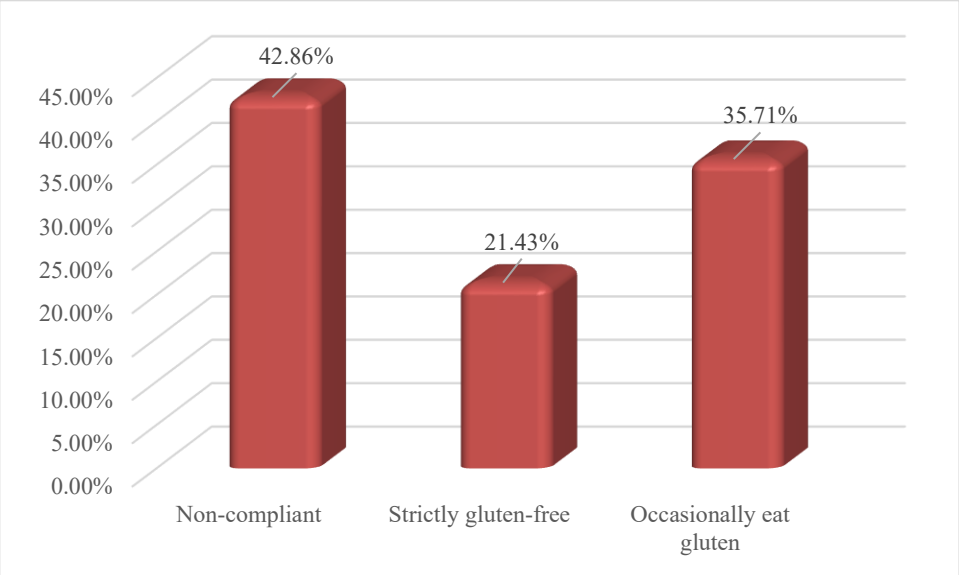


Figure 20: Distribution of Adherence to Dietary Regimen Among Coeliac Patients

Our analysis reveals that the most pressing challenge reported by participants is high cost, affecting 71.43% of them. Other notable difficulties include trouble finding products (53.57%), limited awareness of ingredients (46.43%), and challenges in adhering to the diet (42.86%)(figure 21).

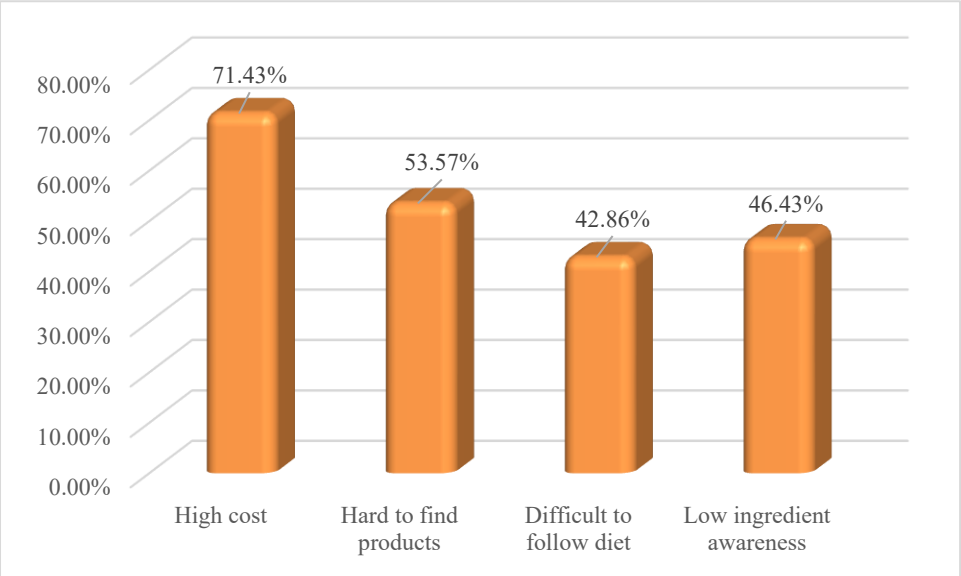


Figure 21: Distribution of Challenges Faced by Coeliac Patients

Our results show that gluten-free bread is the most consumed item among Coeliac patients, with a 100% consumption rate. Following that, gluten-free pastries are chosen by 53.57% of patients, while gluten-free sweets are consumed by 25%(figure 22).

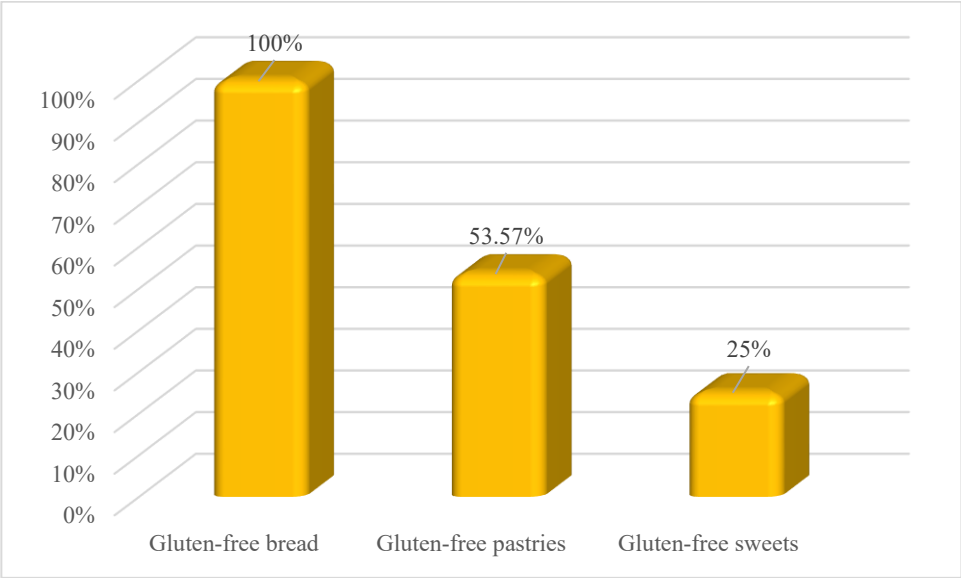


Figure 22: Distribution of Products Consumed by Coeliac Patients

Our analysis highlights that most coeliac patients perceive product prices as High, with 85.71% sharing this view. In contrast, 14.29% regard prices as Medium, while none of the participants considered them to be Low (0%)(figure 23).

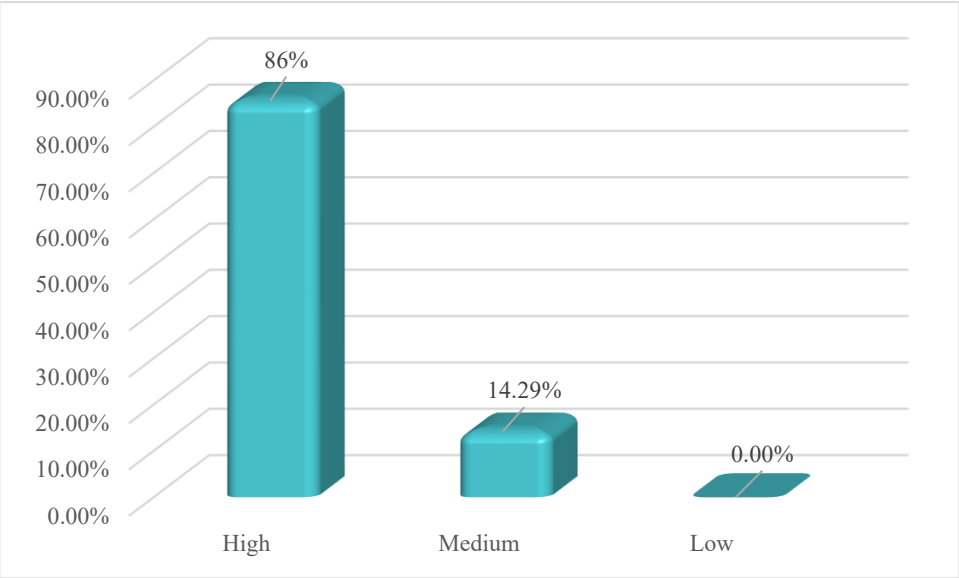


Figure 23: Distribution of Pricing for Gluten-Free Products Among Coeliac Patients

In this study, we carried out a cross-sectional study to assess the prevalence, risk factors, and management of coeliac disease in the city of Guelma (Algeria). While this research provides crucial epidemiological data, it is important to acknowledge certain limitations and biases, particularly those associated with selection bias and the reliance on self-reported symptoms, which could influence the accuracy of the results.

To determine prevalence rates, an anonymous questionnaire was randomly distributed to 300 individuals across several healthcare facilities over a period of two months. Based on the collected data, the prevalence of coeliac disease in the studied population was estimated to be 9.33%(95% CI 6.29 - 13.21).

Several studies have reported coeliac disease prevalence rates that either align with or differ from our findings. For instance, in Algeria multiple studies have reported varying prevalence rates of coeliac disease. Research conducted in Tébessa showed an increase in prevalence from 0.12‰ in 2000 to 1.11‰ in 2014, with an overall average of 0.66‰over 14 years *(Boukezoula, Abla, & Zidoune, 2015).* A broader epidemiological review estimated Algeria's coeliac disease prevalence at 1.43%, positioning the country among those with relatively high gluten intolerance rates *(Ait Idir, 2020).* Moreover, a comparative investigation in Western Algeria examined disease profiles in children versus adults, highlighting differences in symptoms and responses to a gluten-free diet *(Mehadji et al., 2023).*

A recent Italian study estimated that the prevalence of coeliac disease in 2023 was 0.45%, with Aosta Valley, the Autonomous Province of Trento, and Tuscany showing the highest rates, while Marche recorded the lowest at 0.36%*(Gagliardi, 2025).* In contrast, a Moroccan study found an estimated prevalence of 1 per 135 individuals, indicating that regional differences in genetic predisposition, dietary habits, and diagnostic techniques might contribute to variations in disease prevalence *(Haddadi et al., 2023).*

These disparities in prevalence rates across populations can largely be attributed to the limitations of cross-sectional studies, which collect data at a single time point rather than monitoring subjects longitudinally. This methodology may contribute to selection bias and misclassification errors, affecting the accuracy of prevalence estimates *(Savitz & Wellenius, 2022).*

In our study, 12.71% of individuals diagnosed with coeliac disease were female, while 4.20% were male, resulting in a female-to-male ratio of 4.6. This trend is consistent with findings from other studies, where research has shown that women are diagnosed with coeliac disease more frequently than men, with a female-to-male ratio of 1.85:1 *(Jansson-Knodell et al., 2018).*

Our results are similar to the findings in previous studies in Algeria, coeliac disease is more prevalent among women than men, with a female-to-male ratio of 1.62 *(El Mehadji et al., 2023).*

Several factors may explain this disparity, including hormonal influences, genetic susceptibility, diagnostic biases, and environmental factors. Oestrogen modulates immune responses, increasing susceptibility to autoimmune diseases *(Galli et al., 2022).*

Additionally, genetic factors linked to the X chromosome could play a role *(Hernangomez-Laderas et al., 2023).* Women generally seek medical care more frequently, leading to higher diagnosis rates *(Rubio-Tapia et al., 2018).* Environmental aspects such as dietary habits and exposure to triggers may also contribute to gender disparities *(Blanco-García et al., 2025).*

According to the age of patients, it ranged from 9 to 53 years. Participants were grouped into five age categories . The age groups [9–17] and [18–26] each represented 28.57% of the total sample . The highest proportion was recorded in the [27–35] age group, comprising 32.14%. The lowest proportions were recorded in the [36–51] and [45–53] age groups, accounting for 7.14% and 3.57%, respectively. The average age of the participants was 24.36 ± 10.37 years.

Our results align with previous studies conducted in Europe and North Africa, which highlight the significant role of age in coeliac disease prevalence. For instance, research in Algeria suggests that coeliac disease is more commonly diagnosed in children than in adults, indicating potential genetic and regional influences on its distribution *(Singh et al., 2018).*

Meanwhile, in Italy, recent data indicates that 67% of individuals diagnosed with coeliac disease are between 18 and 59 years old, reinforcing the idea that adult diagnosis is more prevalent. Additionally, research confirms that coeliac disease cases in children have doubled over the past 25 years, pointing to an increasing trend in early detection *(Gagliardi, 2025).*

Furthermore, previous studies have focused on high-risk factors associated with coeliac disease, with findings consistently affirming that age plays a crucial role in diagnosis rates *(Collin et al., 2018).*

Regarding our results for BMI distribution among coeliac disease patients, distinct patterns were observed. The majority, 53.57% , maintained a normal BMI ($18.5 \leq BMI < 25$), indicating that most individuals upheld a balanced weight. In contrast, 21.43% were underweight ($BMI < 18$), suggesting that malnutrition or dietary restrictions could be

contributing factors. Interestingly, an equal proportion of 21.43% fell into the overweight category ($25 \leq BMI < 30$), illustrating variability in weight among affected individuals. Meanwhile, only one patient (3.57%) was classified as obese ($BMI \geq 30$), reinforcing that while obesity exists among coeliac patients, it remains relatively uncommon within this sample.

Our findings are consistent with previous studies exploring the connection between coeliac disease and BMI, highlighting the essential role of nutritional status in disease development and progression *(Maleki et al., 2024).* Research has shown that while many coeliac patients maintain a normal weight, others experience weight fluctuations due to malabsorption and dietary adaptations *(Monzani et al., 2024).*

According to the results of the geographical distribution of coeliac disease patients, 78.57% reside in urban areas, whereas 21.42% live in rural regions.

In contrast, studies from Pakistan show that urban patients are diagnosed more frequently, as healthcare facilities in rural areas often lack adequate screening tools *(Bashir et al., 2022).*

The higher prevalence of coeliac disease among urban residents suggests that factors like advanced healthcare infrastructure, greater awareness, and better access to gluten-free products contribute to improved disease detection and dietary adherence *(Posterick & Ayars, 2023).*

Conversely, rural patients experience significant barriers, including lower medical support, limited knowledge, and restricted food availability, which can lead to undiagnosed or poorly managed cases*(Howell, 2018).*

For the results of diagnosis locations among coeliac patients . The majority, 71.43% of cases, were diagnosed at a gastroenterologist's clinic. Additionally, 17.86% of diagnoses occurred in general practitioners' clinics. Meanwhile, 10.71% of patients received their diagnosis at a hospital or medical centre.

Similarly, research suggests that primary care practitioners are increasingly involved in recognising early symptoms, leading to more diagnoses initiated in general practice before specialist referral *(Ludvigsson et al., 2014).*

Meanwhile, findings indicate that hospital-based diagnoses are relatively uncommon, as most cases are identified through outpatient consultations rather than inpatient care *(Ludvigsson et al., 2014).*

The results concerning diagnostic methods for coeliac disease reveal significant variability in approaches. In our study, intestinal biopsy was the most frequently utilized

method, performed in 53.57% of patients. Additionally, 25% of patients received a diagnosis through blood tests, while 21.43% were diagnosed based on clinical symptoms.

Multiple studies confirm that diagnostic variability plays a crucial role in coeliac disease detection*(Arguelles-Grande et al., 2011)*. Although biopsy remains the most definitive method, there is a gradual shift toward less invasive techniques, such as serological screening and genetic testing. Standardizing diagnostic approaches could enhance accuracy, early detection, and patient outcomes *(Elwenspoek et al., 2021).*

The results regarding the onset age of coeliac disease reveal considerable variation among patients. In our study, the age at diagnosis ranged from 1 to 30 years, with an average onset age of 11.39 ± 7.93 years. The majority (53.57%) developed the disease between 1 and 10 years, while 25% were diagnosed between 11 and 20 years. Additionally, 21.43% of cases experienced disease onset between 21 and 30 years .

Findings indicate that coeliac disease can develop at any age, but the highest prevalence occurs in childhood and early adulthood *(Caio et al., 2019).* These results align with the current study, where the majority of cases were diagnosed before adulthood *(Villanueva et al., 2020).*

Results of this study indicate that coeliac disease often manifests in childhood but may also develop later during adolescence or adulthood, influenced by genetic and environmental factors.The immune system in children is more sensitive to gluten, leading to an earlier onset of symptoms, while hormonal changes and dietary shifts can trigger the disease at later stages. Some cases remain undetected for years until factors such as infections or stress activate the condition *(Villanueva et al., 2020).*

According to the results concerning clinical manifestations of coeliac disease All patients (100%) in our study experienced gastrointestinal symptoms. Additionally, 21.43% reported weight loss, while 28.57%suffered from persistent fatigue . Abdominal pain was observed in 14.29% of patients, and 17.86% reported skin problems, such as rashes. Furthermore, 10.71% experienced hair loss. Other symptoms were reported by 7.14%.

Studies indicate that coeliac disease primarily affects the digestive system, with common symptoms including chronic diarrhea, anemia, and weight loss *(Sharma et al., 2020).* However, some patients experience extraintestinal complications. Non-classical symptoms, such as chronic fatigue and dermatological issues, are prevalent among adults with the disease, with persistent exhaustion and skin rashes linked to autoimmune disorders *(Rossi et al., 2024).*

Research indicates that coeliac disease primarily affects the digestive system, leading to malabsorption and gastrointestinal disturbances, with symptoms such as chronic diarrhea and anemia being the most common *(Sharma et al., 2020).* Additionally, impaired nutrient absorption contributes to chronic fatigue and weight loss, impacting overall health *(Rossi et al., 2024).* Beyond digestion, the disease manifests in extraintestinal complications, including skin conditions and oral health issues like mouth ulcers, enamel defects, and tongue pain, likely due to an abnormal immune response *(Manninen et al., 2025).*

The results regarding family history of coeliac disease demonstrate a strong hereditary component. In our study, 21.42% of participants reported having at least one affected family member. The prevalence among those with an affected sister was 50%, while 33.33% had an affected cousin and 16.67% had an affected brother, emphasizing the familial clustering of the disease.

These findings align with previous research on familial prevalence of coeliac disease, which indicates that first-degree relatives are at an increased risk of developing the condition, particularly among siblings and parents *(Airaksinen et al., 2021).* Similarly, our results reinforce the notion that genetic predisposition plays a crucial role in disease manifestation, supporting existing studies linking HLA-DQ2.5 and HLA-DQ8 genetic markers to increased susceptibility *(Aitella et al., 2025).*

For the result of the comorbidities among coeliac disease patients, anaemia was found to be the most prevalent condition, affecting 81.82% of individuals. In contrast, diabetes was diagnosed in only 18.18% of patients.

The high prevalence of anaemia among coeliac patients supports the hypothesis that nutritional deficiencies and malabsorption play a crucial role in disease progression *(Seidita et al., 2022).* Additionally, persistent cases of anaemia despite adherence to a gluten-free diet suggest that dietary interventions alone may not fully correct iron deficiency *(Valvano et al., 2025).*

The lower prevalence of diabetes compared to anaemia indicates that while coeliac disease and type 1 diabetes share genetic predispositions, their co-occurrence remains relatively uncommon *(Malekahmadi et al., 2024).*

According to the results of our study, dietary adherence among coeliac disease patients presents a significant concern, with 42.86% struggling with non-compliance, while 35.71% report occasional gluten consumption. Interestingly, only 21.43% maintain strict adherence.

Our results emphasize the global challenges associated with maintaining dietary restrictions for coeliac patients. Social influences, economic factors, and accessibility issues significantly impact dietary adherence *(Jeanes et al., 2019).*

For the result of the c hallenges in maintaining a strict gluten-free diet, our study highlights key difficulties faced by coeliac patients. The most commonly reported issue was high cost, affecting 71.43% of participants, while 53.57% struggled with finding gluten-free products.Another key challenge was limited awareness of ingredients, affecting 46.43% of individuals. Lastly, 42.86% of patients reported difficulty adhering to the diet.

A study conducted in India found that high costs and limited product availability were primary concerns for coeliac patients, confirming the financial and accessibility barriers reported in our study *(Domma et al., 2022).* Similarly, research from Canada revealed that confusing food labels made it difficult for patients to identify safe products, supporting our findings regarding ingredient awareness *(Gutowski et al., 2018).*

These results highlight the significant challenges faced by individuals managing celiac disease. The high cost of gluten-free products is a significant obstacle, especially in areas with limited access to specialized foods. Additionally, scarcity of gluten-free options makes dietary adherence challenging. Poor food labeling and lack of ingredient awareness further increase the risk of unintentional gluten exposure for patients *(Payette et al., 2025).*

For the results concerning the consumption of gluten-free products among coeliac patients, our study found that gluten-free bread is the most frequently consumed item, with all participants reporting regular intake. In contrast, gluten-free pastries (53.57%) and sweets (25%) were consumed less frequently, reflecting varying dietary preferences within this group.

Several studies support these findings, indicating that gluten-free bread remains a staple despite widespread dissatisfaction with its texture and taste, suggesting that necessity often outweighs preference *(Dean et al., 2024).* Gluten-free pastries tend to be more expensive, affecting purchasing decisions and limiting accessibility for certain consumers *(Bauner et al., 2022).* Meanwhile, gluten-free sweets are often chosen based on health and taste considerations, with increasing demand for better-quality alternatives *(Toth et al., 2020).*

These results indicate that dietary choices among coeliac patients are shaped by necessity, cost, and quality expectations, with staple foods such as bread remaining central, while pastries and sweets are influenced by economic and nutritional factors *(Dean et al., 2024; Bauner et al., 2022; Toth et al., 2020).*

For the result of gluten-free product pricing among coeliac disease patients, our study highlights a notable concern, with 85.71% perceiving the costs as high, while 14.29% regard them as medium. Interestingly, none of the participants considered gluten-free product prices to be low.

Examining studies from other regions, researchers in Algeria found that gluten-free product prices are two to six times higher than regular food products, posing a significant financial challenge for coeliac patients *(Bouasla et al., 2025).*

The study indicates that the high cost of gluten-free products presents a major challenge for coeliac patients, as many struggle to afford them. This price increase is due to high production costs, limited availability, and the use of specialized ingredients to ensure gluten-free certification *(Bouasla et al., 2025).*

Conclusion

Conclusion

Coeliac disease is a prevalent autoimmune disorder that poses significant health challenges, particularly in genetically predisposed individuals. This cross-sectional study has provided valuable insights into the prevalence, risk factors, and management of coeliac disease within the population of Guelma.

Despite several challenges in the research process, the study successfully identified key associations between demographic characteristics, environmental influences, and disease occurrence. The findings indicate that the prevalence of coeliac disease in Guelma is 9.33% (95% CI 6.29 - 13.21), with the most affected age group being 9–17 years. High-risk groups include individuals with a family history of coeliac disease, those with nutritional deficiencies, and individuals experiencing persistent gastrointestinal symptoms. Additionally, factors such as low awareness of gluten sources, limited access to gluten-free products, and high costs were found to contribute to challenges in disease management.

These results highlight the importance of early diagnosis and dietary intervention to prevent complications such as osteoporosis, anemia, and intestinal malignancies. Public health strategies should focus on raising awareness, improving access to gluten-free products, and enhancing diagnostic capabilities to support affected individuals.

Addressing these factors through comprehensive healthcare policies can significantly improve the quality of life for coeliac patients in Guelma. Furthermore, targeted education programs could play a crucial role in reducing misconceptions about gluten intolerance and promoting effective disease management.

Perspectives and Limitations

This descriptive cross-sectional study provides valuable insights into the prevalence, risk factors, and management of coeliac disease within the population of Guelma. However, given the nature of cross-sectional research, the study identifies associations rather than establishes causality. This means that while key risk factors have been highlighted, they cannot be definitively confirmed as causal contributors to the development of coeliac disease.

Throughout the research process, we encountered several challenges in data collection, particularly the low response rate to the questionnaire. Many individuals hesitated to participate or provide detailed answers, which affected the accuracy of reported data and may have introduced recall bias participants may not accurately remember or report past dietary habits, symptoms, or exposure to risk factors.

Additionally, the sample size of 300 participants, while sufficient for preliminary analysis, may not be large enough to generalize findings to the entire population of Guelma. Expanding the sample size would enhance statistical power and improve external validity, ensuring that the results better reflect broader demographic patterns. Furthermore, applying advanced statistical methods, such as multivariate logistic regression analysis, could refine the relationship between independent variables and disease prevalence.

Despite these limitations, the study successfully identified critical risk factors, including genetic predisposition (HLA-DQ2/DQ8), dietary habits, and socioeconomic barriers affecting access to gluten-free foods. These findings emphasize the need for early screening and intervention programs aimed at improving disease management and awareness.

To enhance the accuracy of the study's findings, we propose conducting the practical component in a hospital setting, where medical examinations can be performed directly on participants. This approach would enable more precise and comprehensive data collection, covering both clinical diagnosis and laboratory analyses. Implementing this step would help reduce potential biases associated with questionnaires and improve the validity of findings related to disease prevalence and risk factors.

List of references

- **Äärelä, L., Nurminen, S., Kivelä, L., Huhtala, H., Mäki, M., & Kurppa, K. (2016).** Prevalence and associated factors of abnormal liver values in children with celiac disease. Digestive and Liver Disease, 48(9), 1023–1029.
- **Abed, N., Bouzaroura, I., & Guergour, A. (2023).** Characteristics of adult celiac disease in Eastern Algeria. Journal of Biomedical and Clinical Research, 16(1), 25–32.
- **Aboulaghras, S., Piancatelli, D., Taghzouti, K., Balahbib, A., Alshahrani, M. M., Al Awadh, A. A., Goh, K. W., Ming, L. C., Bouyahya, A., & Oumhani, K. (2023).** Meta-analysis and systematic review of HLA DQ2/DQ8 in adults with celiac disease. International Journal of Molecular Sciences, 24(2), 1188.
- **Abu Daya, H., Lebwohl, B., Lewis, S. K., & Green, P. H. R. (2013).** Celiac disease patients presenting with anemia have more severe disease than those presenting with diarrhea. Clinical Gastroenterology and Hepatology, 11(11), 1472-1477.
- **Adams, D. (2022).** Celiac disease may put patients at risk for avoidant/restrictive food disorder. Gastro Hep Advances.
- **Airaksinen, L., Myllymäki, L., Kaukinen, K., Saavalainen, P., Huhtala, H., Lindfors, K., & Kurppa, K. (2021).** Differences between familial and sporadic celiac disease. Digestive Diseases and Sciences, 66, 1981–1988.
- **Ait Idir, K. (2020).** Épidémiologie de la maladie cœliaque dans le monde. Batna Journal of Medical Sciences, 7(1), 1-5.
- **Aitella, E., Cozzolino, D., Ginaldi, L., & Romano, C. (2025).** Celiac Disease: A Transitional Point of View. Nutrients, 17(2), 234.
- **Al Kindi, R., Al Salmani, A., Al Hadhrami, R., & Al Maashani, M. (2023).**Epidemiology of celiac disease. In Celiac Disease and Gluten-Free Diet (Ed. L. Rodrigo). IntechOpen.
- **Al-Toma, A., Volta, U., Auricchio, R., Castillejo, G., Sanders, D. S., Cellier, C., Mulder, C. J., & Lundin, K. E. A. (2019).** European Society for the Study of Coeliac Disease (ESsCD) guideline for coeliac disease and other gluten-related disorders. United European Gastroenterology Journal, 7(5), 583–613.
- **Andersen, V., Möller, S., Jensen, P. B., Møller, F. T., & Green, A. (2020).** Caesarean delivery and risk of chronic inflammatory diseases (Inflammatory bowel disease, rheumatoid arthritis, coeliac disease, and diabetes mellitus): A population-based

registry study of 2,699,479 births in Denmark during 1973–2016. Clinical Epidemiology, 12, 287-293.

- **Arguelles-Grande, C., Tennyson, C. A., Lewis, S. K., Green, P. H., & Bhagat, G. (2012).**Variability in small bowel histopathology reporting between different pathology practice settings: impact on the diagnosis of coeliac disease. Journal of Clinical Pathology, 65(3), 242-247.
- **Asma, A., Al Kindi, R., Al Hadhrami, R., & Al Maashani, M. (2023).** Epidemiology of celiac disease. IntechOpen.
- **Barone, M. V., & Auricchio, S. (2021).** A cumulative effect of food and viruses to trigger celiac disease (CD): A commentary on the recent literature. International Journal of Molecular Sciences, 22(4), 2027.
- **Barone, M., Iannone, A., Cristofori, F., Dargenio, V. N., Indrio, F., Verduci, E., Di Leo, A., & Francavilla, R. (2023).**Risk of obesity during a gluten-free diet in pediatric and adult patients with celiac disease: A systematic review with meta-analysis. Nutrition Reviews, 81(3), 252-266.
- **Bascuñán, K. A., Vespa, M. C., & Araya, M. (2017).** Celiac disease: Understanding the gluten-free diet. European Journal of Nutrition, 56(2), 449-459.
- **Bauner, C., & Lavoie, N. (2022).** The costs of eating gluten-free. University of Massachusetts Amherst.
- **Berry, S. D., Dufour, A. B., Travison, T. G., et al. (2018).** Changes in Bone Mineral Density (BMD): A Longitudinal Study of Osteoporosis Patients in the Real-World Setting. Archives of Osteoporosis, 13, 124.
- **Bianchi, P. I., Lenti, M. V., Petrucci, C., Gambini, G., Aronico, N., & Varallo, M. (2024).** Diagnostic delay of celiac disease in childhood. JAMA Network Open, 7(4), e245671.
- **Blanco-García, A., López-Hoyos, M.,Irure-Ventura, J., & Muñoz-Cacho, P.(2025).** Epidemiology of celiac disease in Cantabria, Spain. Diagnostics, 15(505).
- **Bouasla, A., Saouchi, S., Benramoul, K., & Vriesekoop, F. (2025).** Availability and cost of gluten-free products in Algeria. British Food Journal.
- **Boukezoula, F., Abla, K., & Zidoune, M. N. (2015).**La maladie cœliaque à Tébessa (Algérie) : Evolution de la prévalence entre 2000 et 2014. Annales des sciences de la santé, 1(1), 13-19.

- **Bouteloup,C.(2016).** Hypersensibilités et intolérances alimentaires (autres que l'allergie et la maladie cœliaque). Innovations Agronomiques, 52, 15-25.
- **Brown, I. (2016).**Histopathology of celiac disease. Envoi Pathology Update, 7, 1-5.
- **Caio, G., Volta, U., Sapone, A., Leffler, D. A., De Giorgio, R., Catassi, C., & Fasano, A. (2019).** Celiac disease: A comprehensive current review. BMC Medicine, 17(142).
- **Campisi, G., Di Liberto, C., Carroccio, A., Compilato, D., Iacono, G., Procaccini, M., Di Fede, G., Lo Muzio, L., Craxi, A., Catassi, C., & Scully, C. (2007).** Coeliac disease: Oral ulcer prevalence, assessment of risk and association with gluten-free diet in children. Digestive and Liver Disease, 40(1), 104–107.
- **Castillo, N. E., Theethira, T. G., & Leffler, D. A. (2015).** The present and the future in the diagnosis and management of celiac disease. Gastroenterology Report, 3(1), 311.
- **Catassi, C., & Fasano, A. (2012).**The global burden of coeliac disease: Opportunities and challenges.Scientific Research Publishing
- **Catassi, C., Fabiani, E., Iacono, G., D'Agate, C., Francavilla, R., Biagi, F., Volta, U., Accomando, S., Picarelli, A., De Vitis, I., Pianelli, G., Gesuita, R., Carle, F., Mandolesi, A., Bearzi, I., & Fasano, A. (2022).** Toxicity of gluten traces in patients on treatment for celiac disease: A prospective, double-blind, placebo-controlled gluten trial to establish safe gluten threshold. American Journal of Clinical Nutrition, 85(1), 160-166.
- **Catassi, C., Fabiani, E., Iacono, G., De Vitis, I., Pianelli, R., Gesuita, F., Carle, F., Mandolesi, A., Bearzi, I., & Vizzoni, L. (1994).** A prospective, double-blind, placebo-controlled trial to establish a safe gluten threshold for patients with celiac disease. American Journal of Clinical Nutrition, 85(1), 160–166.
- **Catroux, M., Lauda-Maillen, M., Pathe, M., de Ruolz, A. C. D. B., Cazenave-Roblot, F., Roblot, P., & Souchaud-Debouverie, O. (2017).** Événements infectieux survenus au cours des maladies auto-immunes traitées par rituximab: à partir d'une étude rétrospective de 93 cas. La Revue de Médecine Interne, 38(3), 160–166.
- **Cebolla, A., Syage, J. A., Kelly, C. P., Dickason, M. A., Leon, F., Dominguez, R., & Sealey-Voyksner, J. A. (2018).** Determination of gluten consumption in celiac disease patients on a gluten-free diet. American Journal of Clinical Nutrition, 107(2), 201-207.

- **Celdir, M. G., Jansson-Knodell, C. L., Hujoel, I. A., Prokop, L. J., Wang, Z., Murad, M. H., & Murray, J. A. (2021)**. Latitude and celiac disease prevalence: A meta-analysis and meta-regression. Clinical Gastroenterology and Hepatology, 20(6), e1231-e1239.
- **Collin, P., Vilppula, A., Luostarinen, L., Holmes, G. K. T., & Kaukinen, K. (2018).** Review article: Coeliac disease in later life must not be missed. Alimentary Pharmacology & Therapeutics, 47(5), 563-572.
- **Dean, D., Rombach, M., Vriesekoop, F., Mongondry, P., Le Viet, H., Laophetsakunchai, S., Urbano, B., Briz, T., Xhakollari, V., Atasoy, G., Turhan, M., Chrysostomou, S., Hadjimbei, E., Hassan, H., Bassil, M., Arnala, S., Głąbska, D., Guzek, D., van den Berg, S., & Ossel, L. (2024).** Against the grain: Consumer's purchase habits and satisfaction with gluten-free product offerings in European food retail. Foods, 13(19), 3152.
- **DeGaetani, M., Tennyson, C. A., Lebwohl, B., Lewis, S. K., Abu Daya, H., Arguelles-Grande, C., Bhagat, G., & Green, P. H. (2013).** Villous atrophy and negative celiac serology: A diagnostic and therapeutic dilemma. The American Journal of Gastroenterology, 108(5), 647-653.
- **Di Vincenzo, F., Del Gaudio, A., Petito, V., Lopetuso, L. R., & Scaldaferri, F. (2023).** Gut microbiota, intestinal permeability, and systemic inflammation: A narrative review. Internal and Emergency Medicine, 19, 275–293.
  disease in a large at-risk United States population by using HLA alleles. Clin
  Disease Primers, 5(1), 3.
- **Dochat, C., Afari, N., Satherley, R.-M., Coburn, S., & McBeth, J. F. (2024).** Celiac disease symptom profiles and their relationship to gluten-free diet adherence, mental health, and quality of life. BMC Gastroenterology, 24(9).
- **Douida, A., Tahiri, L., Berraho, M., Moustapha, H., Elyousfi, M., Hammas, N., El Fatemi, H., & Chbani, L. (2020).** What is the most reproducible histopathological classification for celiac disease? Study of the interobserver variability in a series of 69 cases. PAMJ Clinical Medicine, 3(2).
- **Du Pré, M. F., Blazevski, J., Dewan, A. E., Stamnaes, J., Kanduri, C., Sandve, G. K., Johannesen, M. K., Lindstad, C. B., Hnida, K., Fugger, L., & Sollid, L. M.**

(2020). B cell tolerance and antibody production to the celiac disease autoantigen transglutaminase 2. Journal of Experimental Medicine, 217(2), e20190860.

- **Dydensborg Sander, S., et al. (2019).** Childhood exposure to systemic antibiotics linked to celiac disease. Gastroenterology. Brown, J. J., Jabri, B., & Dermody, T. S. (2018). A viral trigger for celiac disease. PLOS Pathogens, 14(9), e1007181.
- **Emilsson, L., Semrad, C., Lebwohl, B., Green, P. H. R., & Ludvigsson, J. F. (2020).** Risk of Small Bowel Adenocarcinoma, Adenomas, and Carcinoids in a Nationwide Cohort of Individuals With Celiac Disease. Gastroenterology, 159(5), 1686-1694.e2.
- **Elwenspoek, M. M. C., Jackson, J., O'Donnell, R., Sinobas, A., Dawson, S., Everitt, H., Gillett, P., Hay, A. D., Lane, D. L., Mallett, S., Robins, G., Watson, J. C., Jones, H. E., & Whiting, P. (2021).**The accuracy of diagnostic indicators for coeliac disease: A systematic review and meta-analysis. PLOS ONE, 16(10), e0258501.
- **Gagliardi, J. (2025).** Celiac disease prevalence in Italy 2023, by region. Statista.
- **Galipeau, H. J., & Verdu, E. F. (2014).** Gut microbes and adverse food reactions: Focus on gluten-related disorders. Gut Microbes, 5(5), 594-605.
- **Galli, G., Amici, G., Conti, L., Lahner, E., Annibale, B., & Carabotti, M. (2022).** Sex–gender differences in adult coeliac disease at diagnosis and gluten-free-diet follow-up. Nutrients, 14(15), 3192.
- **Grainge, M. J., West, J., Solaymani-Dodaran, M., Card, T. R., & Logan, R. F. A. (2012).** The long-term risk of malignancy following a diagnosis of coeliac disease or dermatitis herpetiformis: A cohort study. Alimentary Pharmacology & Therapeutics, 35(6), 730–739.
- **Grode, L., Bech, B. H., Jensen, T. M., Humaidan, P., Agerholm, I. E., Plana-Ripoll, O., & Ramlau-Hansen, C. H. (2018).** Prevalence, incidence, and autoimmune comorbidities of celiac disease: A nationwide, population-based study in Denmark from 1977 to 2016. European Journal of Gastroenterology & Hepatology, 30(1), 83-91.
- **Gruver, A. M., Lu, H., Zhao, X., Fulford, A. D., Soper, M. D., Ballard, D., Hanson, J. C., Schade, A. E., Hsi, E. D., Gottlieb, K., & Credille, K. M. (2023).** Pathologist-trained machine learning classifiers developed to quantitate celiac disease features differentiate endoscopic biopsies according to modified Marsh score and dietary intervention response. Diagnostic Pathology, 18, Article 122.

- **Gujral, N., Freeman, H. J., & Thomson, A. B. R. (2012).**Celiac disease: Prevalence, diagnosis, pathogenesis, and treatment. World Journal of Gastroenterology, 18(42), 6036-6059.
- **Gutierrez-Achury, J., Zhernakova, A., Pulit, S. L., Trynka, G., Hunt, K. A., Romanos, J., Raychaudhuri, S., van Heel, D. A., Wijmenga, C., & de Bakker, P. I. W. (2015).** Fine mapping in the MHC region accounts for 18% additional genetic risk for celiac disease. Nature Genetics, 47(6), 592–598.
- **Gutowski, E., Silvester, J., Rigaux, L., Green, K., Weiten, D., Bernstein, C. N., Walker, J. R., Graff, L. A., & Duerksen, D. (2018).** Canadians with celiac disease misinterpret product label information which may lead to unsafe food choices despite allergen labelling laws. Journal of the Canadian Association of Gastroenterology, 1(suppl_2), 254.
- **Haddadi, M., Mellouki, I., Benmakhlouf, Y., Diakite, A., Khaili, A., Barrijal, S., & Essalmani, H. (2023).** Epidemiology of Celiac Disease in Northern Morocco in 2018–2021: A Descriptive Cross-Sectional Study. Kesmas: National Public Health Journal, 18(5), 49-54.
- **Hadjivassiliou, M., Sanders, D. S., Grünewald, R. A., Woodroofe, N., Williamson, C., & Croall, I. (2010).** Gluten sensitivity: From gut to brain. The Lancet Neurology, 9(3), 318-330.
- **Heikkilä, K., Pearce, J., Mäki, M., & Kaukinen, K. (2015).** Celiac disease and bone fractures: A systematic review and meta-analysis. The Journal of Clinical Endocrinology & Metabolism, 100(1), 25–34.
- **Hernangomez-Laderas,A., Cilleros-Portet, A., Martínez Velasco, S., Marí, S., Legarda, M., González-García, B. P., Tutau, C., García-Santisteban, I., Irastorza, I., Fernandez-Jimenez, N., & Bilbao, J. R. (2023).** Sex bias in celiac disease: XWAS and monocyte eQTLs in women identify TMEM187 as a functional candidate gene. Biology of Sex Differences, 14, Article 86.
- **Hervonen, K., Karell, K., Holopainen, P., Collin, P., Partanen, J., & Reunala, T. (2000).** Concordance of dermatitis herpetiformis and celiac disease in monozygous twins. Journal of Investigative Dermatology, 115(6), 990–993.

- **Howell, R. (2018).** Experiences with celiac disease for those in rural versus urban areas of Western North Carolina (Unpublished honors thesis). Appalachian State University, Boone, NC.
- **Ilus, T., Kaukinen, K., Virta, L. J., Pukkala, E., & Collin, P. (2014).** Incidence of malignancies in diagnosed celiac patients: A population-based estimate. American Journal of Gastroenterology, 109(9), 1471-1477.
- **Infantino, C., Francavilla, R., Vella, A., Cenni, S., Principi, N., Strisciuglio, C., & Esposito, S. (2022).** Role of vitamin D in celiac disease and inflammatory bowel diseases. Nutrients, 14(5154).
- **Iversen, R., & Sollid, L. M. (2020).** The immunobiology and pathogenesis of celiac disease. Annual Review of Pathology: Mechanisms of Disease, 18, 47-70.
- **Jansson-Knodell, C. L., King, K. S., Larson, J. J., Van Dyke, C. T., Murray, J. A., & Rubio-Tapia, A. (2018).** Gender-based differences in a population-based cohort with celiac disease: More alike than unalike. Digestive Diseases and Sciences, 63(11), 2821–2828.
- **Jeanes, Y., Reeves, S., Muhammad, H., Mayberry, J., & Ishaq, S. (2019).** Intervention improves knowledge of gluten-free foods and dietary adherence in adults with coeliac disease. School of Life and Health Sciences.
- **Jericho, H., Sansotta, N., & Guandalini, S. (2017).** Extraintestinal manifestations of celiac disease: Effectiveness of the gluten-free diet. Journal of Pediatric Gastroenterology and Nutrition, 65(1), 75-79.
- **Kamer, J. H., Weijers, H. A., & Dicke, W. K. (1953).** Coeliac disease. IV. An investigation into the injurious constituents of wheat in connection with their action on patients with coeliac disease. Acta Paediatrica, 42(3), 223-231.
- **Kårhus, L. L., Gunnes, N., Størdal, K., Bakken, I. J., Tapia, G., & Stene, L. C. (2018).** Influenza and risk of later celiac disease: A cohort study of 2.6 million people. Scandinavian Journal of Gastroenterology, 53(1), 15–23.
- **Kivelä, L., & Kurppa, K. (2018).**Extraintestinal manifestations of celiac disease: Early detection for better long-term outcomes. Nutrients, 10(8), 1015.
- **Kivelä, L., Caminero, A., Leffler, D. A., Pinto-Sanchez, M. I., Tye-Din, J. A., & Lindfors, K. (2021).** Current and emerging therapies for coeliac disease. Nature Reviews Gastroenterology & Hepatology, 18, 181–195.

- **Kivelä, L., Kurppa, K., Kaukinen, K., Tauschi, R., Eurén, A., Vuorela, N., Koskimaa, S., Huhtala, H., & the TEDDY Study Group. (2022).** Association of concomitant autoimmunity with the disease features and long-term treatment and health outcomes in celiac disease. Frontiers in Medicine, 9, 1055135.
- **Kowsari, K., Sali, R., Khan, M. N., Adorno, W., Ali, S. A., Moore, S. R., Amadi, B. C., Kelly, P., Syed, S., & Brown, D. E. (2019).** Diagnosis of celiac disease and environmental enteropathy on biopsy images using color balancing on convolutional neural networks. arXiv preprint arXiv:1904.05773.
- **Kurppa, K., Lauronen, O., Collin, P., Ukkola, A., Laurila, K., Huhtala, H., Mäki, M., & Kaukinen, K. (2012).** Factors associated with dietary adherence in celiac disease: A nationwide study. Digestion, 86(4), 309–314.
- **Larussa, T., Suraci, E., Imeneo, M., Marasco, R., & Luzza, F. (2017).** Normal bone mineral density associates with duodenal mucosa healing in adult patients with celiac disease on a gluten-free diet. Nutrients, 9(2), 98.
- **Laurikka, P., Nurminen, S., Kivelä, L., & Kurppa, K. (2018).** Extraintestinal manifestations of celiac disease: Early detection for better long-term outcomes. Nutrients, 10(8), 1015.
- **Lebwohl, B., Ludvigsson, J. F., & Green, P. H. (2015).** Celiac disease and non-celiac gluten sensitivity. BMJ, 351,h4347.
- **Lee, A. R., Wolf, R. L., Lebwohl, B., Ciaccio, E. J., & Green, P. H. R. (2019).** Persistent economic burden of the gluten-free diet. Nutrients, 11(2), 399.
- **Leffler, D. A., Kelly, C. P., Green, P. H. R., Fedorak, R. N., DiMarino, A., Perrow, W., Rasmussen, H., Wang, C., Bercik, P., Bachir, N. M., & Murray, J. A. (2015).** Larazotide Acetate for Persistent Symptoms of Celiac Disease Despite a Gluten-Free Diet: A Randomized Controlled Trial. Gastroenterology, 148(6), 1311-1319.
- **Lepers, S., Couignoux, S., Colombel, J. F., & Dubucquoi, S. (2004).** Celiac disease in adults: New aspects. La Revue de Médecine Interne, 25(1), 22-34.
- **Lindfors, K., Ciacci, C., Kurppa, K., Lundin, K. E. A., Makharia, G. K., Mearin, M. L., Murray, J. A., Verdu, E. F., and Kaukinen, K. (2019).** Coeliac disease. Nature Reviews. Disease Primers, 5(1), 3.
- **Lindfors, K., Lin, J., Lee, H. S., Hyöty, H., Nykter, M., Kurppa, K., Liu, E., Koletzko, S., Rewers, M., Hagopian, W., Toppari, J., Ziegler, A. G., Akolkar, B.,**

Krischer, J. P., Petrosino, J. F., Lloyd, R. E., Agardh, D., & the TEDDY Study Group. (2020). Metagenomics of the faecal virome indicate a cumulative effect of enterovirus and gluten amount on the risk of coeliac disease autoimmunity in genetically at-risk children: The TEDDY study. Gut, 69(8), 1416–1422.

- **Lionetti, E., & Catassi, C. (2011).**New clues in celiac disease epidemiology, pathogenesis, clinical manifestations, and treatment.International Review of Immunology.
- **Lionetti, E., Castellaneta, S., Francavilla, R., Pulvirenti, A., Tonutti, E., Amarri, S., Barbato, M., Barbera, C., Barera, G., Bellantoni, A., Castellano, E., Guariso, G., Limongelli, M. G., Pellegrino, S., Polloni, C., Ughi, C., Zuin, G., Fasano, A., & Catassi, C. (2014).** Introduction of gluten, HLA status, and the risk of celiac disease in children. The New England Journal of Medicine, 371(14), 1295-1303.
- **Liu, E., Dong, F., Barón, A. E., Taki, I., Norris, J. M., Frohnert, B. I., Hoffenberg, E. J., & Rewers, M. (2017).** High incidence of celiac disease in a long-term study of adolescents with susceptibility genotypes. Gastroenterology, 152(6), 1329-1336.e1.
- **Ludvigsson, J. F., Bai, J. C., Biagi, F., Card, T. R., Ciacci, C., Ciclitira, P. J., Green, P. H. R., Hadjivassiliou, M., Holdoway, A., van Heel, D. A., Kaukinen, K., Leffler, D. A., Leonard, J. N., Lundin, K. E. A., McGough, N., Davidson, M., Murray, J. A., Swift, G. L., Walker, M. M., Zingone, F., & Sanders, D. S. (2014).** Diagnosis and management of adult coeliac disease: Guidelines from the British Society of Gastroenterology. Gut, 63(8), 1210–1228.
- **Ludvigsson, J. F., Rubio-Tapia, A., van Dyke, C. T., Melton, L. J., Zinsmeister, A. R., & Murray, J. A.(2013).** Increasing incidence of celiac disease in a North American population. American Journal of Gastroenterology, 108(5), 818-824.
- **Makharia, G. K., Chauhan, A., Singh, P., & Ahuja, V. (2022).** Review article: Epidemiology of coeliac disease. Alimentary Pharmacology & Therapeutics, 56(5), 467–486.
- **Malamut, G., Meresse, B., Cellier, C., & Cerf-Bensussan, N. (2009).** Celiac disease in 2009: A future without gluten-free diet? Gastroentérologie Clinique et Biologie, 33(8-9), 635-647.

- **Malekahmadi, S., Asri, N., Forouzesh, F., Saneifard, H., Rezaei-Tavirani, M., & Rostami-Nejad, M. (2024).** Evaluation of genetic association between celiac disease and type 1 diabetes. Journal of Diabetes & Metabolic Disorders, 23, 1329–1336.
- **Maleki, F., Hosseinpour, M., Delpisheh, A., Bahardoust, M., Hajizadeh-Sharafabad, F., & Pashaei, M. R. (2024).**The prevalence of obesity and underweight in celiac patients at the time of diagnosis: A systematic review and meta-analysis. BMC Gastroenterology, 24(357).
- **Manninen, J., Paavola, S., Kurppa, K., Huhtala, H., Salmi, T., Kaukinen, K., & Pasternack, C. (2025).**Prevalence of oral manifestations in coeliac disease and associated factors. BMC Gastroenterology, 25(126).
- **Mehadji, D., Noria, H., Yekrou, D., Charef, L., Bouziane Nedjadi, K., Ouali, S., Hamri, W. H., Benaissa, Z., & Sellam, F. (2023).** Comparative Profile of Celiac Disease Between Children and Adults in Western Algeria Region. Zahedan Journal of Research in Medical Sciences, 25(3), e126906.
- **Molkhou, P. (2016).**La sensibilité au gluten non maladie cœliaque. Où en sommes-nous en 2016? Revue Française d'Allergologie, 56(7-8), 556-561.
- **Monzani, A., Marcolin, S., Medina, F., Valentino, K., & Rabbone, I. (2024).** BMI status of children with celiac disease has changed in the last decades: A 30-year retrospective study. Nutrients, 16(16), 2729.
- **Mubarak, A., Spierings, E., Wolters, V. M., et al. (2013).** Children with celiac disease and high tTGA are genetically and phenotypically different. World Journal of Gastroenterology, 19(41), 7114–7120.
- **Murray, J. A., Verdu, E. F., and Kaukinen, K. (2019).** Coeliac disease. Nature Reviews.
- **Nurminen, S., Kivelä, L., Huhtala, H., Kaukinen, K., & Kurppa, K. (2019).** Extraintestinal manifestations were common in children with coeliac disease and were more prevalent in patients with more severe clinical and histological presentation.Acta Paediatrica, 108(4), 681-687.
- **Pavan, D., Anaghasree, Satish, P., Chaitanya, D., & Pooja, Y. (2022).**Gluten-free diet: Challenges faced by celiac disease patients. The Pharma Innovation Journal, 11(6S), 2371

- **Payette, C. C., Desjardins, C., Lalanne, E., Marquis, M., & Perreault, M. (2025).**Exploring challenges faced by adults living with celiac disease: A food literacy perspective. Journal of Human Nutrition and Dietetics, 38(2), 215-230.
- **Pekki, H., Kurppa, K., Mäki, M., Huhtala, H., Sievänen, H., Laurila, K., Collin, P., & Kaukinen, K. (2015).** Predictors and significance of incomplete mucosal recovery in celiac disease after 1 year on a gluten-free diet. The American Journal of Gastroenterology, 110, 1078-1085.
- **Pietzak MM, Schofield TC, McGinniss MJ, Nakamura RM (2009).**Stratifying risk for celiac disease in a large at-risk United States population by using HLA alleles. Clin Gastroenterol Hepatol 7:966-971.
- **Posterick, A., & Ayars, C. L. (2023).** Celiac Disease Dietary Adherence on the Rural–Urban Continuum. Nutrients, 15(21), 4535.
- **Raiteri, A., Granito, A., Giamperoli, A., Catenaro, T., Negrini, G., & Tovoli, F. (2022).** Current guidelines for the management of celiac disease: A systematic review with comparative analysis. World Journal of Gastroenterology, 28(1), 154-175.
- **Repo, M., Lindfors, K., Mäki, M., Huhtala, H., Laurila, K., Lähdeaho, M.-L., Saavalainen, P., Kaukinen, K., & Kurppa, K. (2017).** Anemia and Iron Deficiency in Children with Potential Celiac Disease. Journal of Pediatric Gastroenterology and Nutrition, 64(1), 56-62.
- **Romanos, J., Rosén, A., Magadi Gopalaiah, V. K., Trynka, G., Franke, L., Szperl, A., Gutierrez Achury, J., van Diemen, C. C., Kanninga, R., Jankipersadsing, S. A., Steck, A., Eisenbarth, G., van Heel, D. A., Cukrowska, B., Bruno, V., Mazzilli, M. C., Núñez, C., Ramon Bilbao, J., Mearin, M. L., & PreventCD Group. (2014).** Improving coeliac disease risk prediction by testing non-HLA variants additional to HLA variants. Gut, 63(3), 415-422.
- **Rossi, R. E., Masoni, B., Zullo, A., De Deo, D., Hassan, C., & Repici, A. (2024).** Clinical presentation of celiac disease in adult patients: current real-life experience. Internal and Emergency Medicine, 19, 1897–1903.
- **Rostami-Nejad, M., Asri, N., Bakhtiari, S., Khalkhal, E., Maleki, S., Rezaei-Tavirani, M., Jahani-Sherafat, S., & Rostami, K. (2024).** Metabolomics and lipidomics signature in celiac disease: A narrative review. Rostom, A., Murray, J. A., & Kagnoff, M. F. (2006). American Gastroenterological Association (AGA) Institute

Technical Review on the Diagnosis and Management of Coeliac Disease. Gastroenterology, 131(11), 1981-2002.

- **Rotondi Aufiero, V., Iacomino, G., Picariello, E., Troncone, R., & Mazzarella, G. (2025).** Neutralizing IL-15 inhibits tissue-damaging immune response in ex vivo cultured untreated celiac intestinal mucosa. Cells, 14(3), 234.
- **Rubio-Tapia, A., Kyle, R. A., Kaplan, E. L., Johnson, D. R., Page, W., & Melton, L. J.(2012).** Increased prevalence and mortality in undiagnosed celiac disease. Gastroenterology, 142(5), 1129-1136.
- **Rubio-Tapia, A., Ludvigsson, J. F., Van Dyke, C. T., Melton, J. L., Zinsmeister, A. R., Lahr, B. D., & Murray, J. A. (2013).** Increasing incidence of celiac disease in a North American population. The American Journal of Gastroenterology, 108(5), 818–824.
- **Sali, R., Ehsany, L., Kowsari, K., Khany, M., Moskaluky, C. A., Syedy, S., & Brown, D. E. (2019).** CeliacNet: Celiac disease severity diagnosis on duodenal histopathological images using deep residual networks. arXiv preprint arXiv:1910.03084.
- **Sallese, M., Efthymakis, K., Marchioni, M., Neri, B., Dufrusine, B., Dainese, E., Di Nicola, M., & Neri, M. (2023).** Gene expression profiling in coeliac disease confirmed the key role of the immune system and revealed a molecular overlap with non-celiac gluten sensitivity. International Journal of Molecular Sciences, 24(9), 7769.
- **Salmi, T. T., Hervonen, K., Kaukinen, K., & Collin, P. (2015).** Dermatitis herpetiformis as a cutaneous manifestation of celiac disease. British Journal of Dermatology.
- **Savitz, D. A., & Wellenius, G. A. (2022).** Can cross-sectional studies contribute to causal inference? It depends. American Journal of Epidemiology, 192(4), 514–516.
- **Schuppan, D., Mäki, M., Lundin, K. E. A., Isola, J., Friesing-Sosnik, T., Taavela, J., Popp, A., Koskenpato, J., Langhorst, J., Hovde, Ø., Lähdeaho, M.-L., Fusco, S., Schumann, M., Török, H. P., Kupcinskas, J., Zopf, Y., Lohse, A. W., Scheinin, M., Kull, K., Biedermann, L., Byrnes, V., Stallmach, A., Jahnsen, J., Zeitz, J., Mohrbacher, R., & Greinwald, R. (2021).** A randomized trial of a transglutaminase 2 inhibitor for celiac disease. The New England Journal of Medicine, 385, 35-45.
- **See JA, Kaukinen K, Makharia GK, Gibson PR and Murray JA (2015):** Practical

insights into gluten-free diets. Nat Rev Gastroenterol Hepatol 12:580-91.

- **Seidita, A., Mansueto, P., Compagnoni, S., Castellucci, D., Soresi, M., Chiarello, G., et al. (2022).** Anemia in Celiac Disease: Prevalence, Associated Clinical and Laboratory Features, and Persistence after Gluten-Free Diet. Journal of Personalized Medicine, 12(10), 1582.
- **Setty, M., Discepolo, V., Abadie, V., et al. (2015).** Distinct and synergistic contributions of epithelial stress and adaptive immunity to functions of intraepithelial killer cells and active celiac disease. Gastroenterology, 149(1), 681-691.
- **Sharma, N., Bhatia, S., Chunduri, V., Kaur, S., Sharma, S., Kapoor, P., Kumari, A., & Garg, M. (2020).** Pathogenesis of Celiac Disease and Other Gluten Related Disorders in Wheat and Strategies for Mitigating Them. Frontiers in Nutrition, 7(6).
- **Sharp, S. A., Jones, S. E., Kimmitt, R. A., Weedon, M. N., Halpin, A. M., Wood, A. R., Beaumont, R. N., King, S., van Heel, D. A., Campbell, P. M., Hagopian, W. A., Turner, J. M., & Oram, R. A. (2020).** A single nucleotide polymorphism genetic risk score to aid diagnosis of coeliac disease: A pilot study in clinical care. Alimentary Pharmacology & Therapeutics, 52(9), 1231-1242.
- **Shatnawei, A., AlNababteh, A. H., Govender, R. D., Al-Shamsi, S., AlJarrah, A., & Al-Rifai, R. H. (2023).** Mode of presentation and performance of serology assays for diagnosing celiac disease: A single-center study in the United Arab Emirates. Frontiers in Nutrition, 10, 1107017.
- **Singh, P., Arora, S., Lal, S., Strand, T. A., & Makharia, G. K. (2015).** Risk of celiac disease in the first- and second-degree relatives of patients with celiac disease: A systematic review and meta-analysis. The American Journal of Gastroenterology, 110(11), 1539-1548.
- **Singh, P., Arora, A., Strand, T. A., Leffler, D. A., Catassi, C., Green, P. H. R., Kelly, C. P., Ahuja, V., & Makharia, G. K. (2016).** Global prevalence of celiac disease: Systematic review and meta-analysis. Gastroenterology, 151(6), 1101-1109.
- **Singh, P., Arora, A., Strand, T. A., Leffler, D. A., Catassi, C., Green, P. H., Kelly, C. P., Ahuja, V., & Makharia, G. K. (2018).** Global prevalence of celiac disease: Systematic review and meta-analysis. Gastroenterology, 155(3), 887-907.
- **Sollid, L. M. (2002).** Coeliac disease: Dissecting a complex inflammatory disorder. Nature Reviews Immunology, 2(9), 647-655.

- **Sun, Y., Zhou, Q., Tian, D., Zhou, J., & Dong, S. (2024).** Relationship between vitamin D levels and pediatric celiac disease: A systematic review and meta-analysis. BMC Pediatrics, 24, 4688.
- **Syage, J., Ramos, A., Loskutov, V., Norum, A., Bledsoe, A., Choung, R. S., Dickason, M., Sealey-Voyksner, J., & Murray, J. (2023).**Dynamics of serologic change to gluten in celiac disease patients. Nutrients, 15(24), 5083.
- **Taavela, J., Kurppa, K., Jääskeläinen, T., Kaartinen, N. E., Rissanen, H., Huhtala, H., Mäki, M., & Kaukinen, K. (2023).** Trends in the prevalence rates and predictive factors of coeliac disease: A long-term nationwide follow-up study. Alimentary Pharmacology & Therapeutics, 59(3), 372-379.
- **Tersigni, C., Castellani, R., de Waure, C., Fattorossi, A., De Spirito, M., Gasbarrini, A., Scambia, G., & Di Simone, N. (2014).** Celiac disease and reproductive disorders: Meta-analysis of epidemiologic associations and potential pathogenic mechanisms. Human Reproduction Update, 20(4), 582–593.
- **Therrien, A., Silvester, J. A., Leonard, M. M., Leffler, D. A., Fasano, A., & Kelly, C. P. (2020).** Enteric-release budesonide may be useful in the management of non-responsive celiac disease. Digestive Diseases and Sciences, 66, 1989-1997.
- **Thompson, T., & Méndez, E. J. (2008).** Commercial assays to assess gluten content of gluten-free foods: Why they are not created equal. Journal of the American Dietetic Association, 108(10), 1682-1687.
- **Tio, M., Cox, M. R., & Eslick, G. D. (2012).** Meta-analysis: coeliac disease and the risk of all-cause mortality, any malignancy and lymphoid malignancy. Alimentary Pharmacology & Therapeutics, 35(5), 540–551.
- **Tomer, R., Patiyal, S., Dhall, A., & Raghava, G. P. S. (2023).** Prediction of celiac disease-associated epitopes and motifs in a protein. Frontiers in Immunology, 14, 1056101.
- **Toth, M., Vatai, G., & Koris, A. (2020).**Consumers' acceptance, satisfaction in consuming gluten-free bread: A market survey approach. International Journal of Celiac Disease, 8(2), 44-49.
- **Trynka, G., Hunt, K. A., Bockett, N. A., Romanos, J., Mistry, V., Szperl, A., Bakker, S. F., Bardella, M. T., Bhaw-Rosun, L., Castillejo, G., de la Concha, E. G., de Almeida, R. C., Dias, K. R., van Diemen, C. C., Dubois, P. C., Duerr, R. H.,**

Edkins, S., Franke, L., Fransen, K., Gutierrez, J., Heap, G. A., Hrdlickova, B., Hunt, S., Plaza Izurieta, L., Izzo, V., Joosten, L. A., Langford, C., Mazzilli, M. C., Mein, C. A., Midah, V., Mitrovic, M., Mora, B., Morelli, M., Nutland, S., Núñez, C., Onengut-Gumuscu, S., Pearce, K., Platteel, M., Polanco, I., Potter, S., Ribes-Koninckx, C., Ricano-Ponce, I., Rich, S. S., Rybak, A., Santiago, J. L., Senapati, S., Sood, A., Szajewska, H., Troncone, R., Varade, J., Wallace, C., Wolters, V. M., Zhernakova, A., Spanish Consortium on the Genetics of Coeliac Disease (CEGEC), PreventCD Study Group, Wellcome Trust Case Control Consortium (WTCCC), Thelma, B. K., Cukrowska, B., Urcelay, E., Bilbao, J. R., Mearin, M. L., Barisani, D., Barrett, J. C., Plagnol, V., Deloukas, P., Wijmenga, C., & van Heel, D. A. (2011). Dense genotyping identifies and localizes multiple common and rare variant association signals in celiac disease. Nature Genetics, 43(12), 1193-1201.

- **Valvano, M., Longo, S., Stefanelli, G., Frieri, G., Viscido, A., & Latella, G. (2020).** Celiac disease, gluten-free diet, and metabolic and liver disorders. Nutrients, 12(4), 940.
- **Valvano, M., Giansante, C., Vinci, A., Maurici, M., Fabiani, S., Stefanelli, G., Cesaro, N., Viscido, A., Caloisi, C., & Latella, G. (2025).** Persistence of anemia in patients with Celiac disease despite a gluten-free diet: a retrospective study. BMC Gastroenterology, 25(189).
- **Van Bergen, J., Petersen, J., Loh, K. L., Kooy-Winkelaar, Y., Beringer, D. X., Thompson, A., Bakker, S. F., Mulder, C. J. J., Ladell, K., McLaren, J. E., Price, D. A., Rossjohn, J., Reid, H. H., & Koning, F. (2015).** Determinants of gliadin-specific T cell selection in celiac disease. The Journal of Immunology, 194(12), 6112–6122.
- **Verdu, E. F., & Schuppan, D. (2021).** Co-factors, microbes, and immunogenetics in celiac disease to guide novel approaches for diagnosis and treatment. Gastroenterology, 161(5), 1395-1411.e4.
- **Villanueva, M., Oyarzún, A., Leyton, B., González, M., Navarro, E., Canales, P., Ossa, C., Muñoz, M. P., Bascuñán, K. A., & Araya, M. (2020).** Changes in age at diagnosis and nutritional course of celiac disease in the last two decades. Nutrients, 12(1), 156.
- **Vilppula, A., Kaukinen, K., Luostarinen, L., Krekelä, I., Patrikainen, H., Valve, R., Luostarinen, M., Laurila, K., Mäki, M., & Collin, P. (2011).** Clinical benefit of

gluten-free diet in screen-detected older celiac disease patients. BMC Gastroenterology, 11, 136.

- **Volta, U., De Giorgio, R., Caio, G., & Tovoli, F. (2014).** Non-celiac gluten sensitivity: Why worry?BMC Medicine, 12, 86.
- **Volta, U., Fabbri, A., Parisi, C., Piscaglia, M., Caio, G., Tovoli, F., & De Giorgio, R. (2014).** Old and new serological tests for celiac disease screening: A comparison. World Journal of Gastroenterology, 20(12), 4063-4071.
- **Vriesekoop, F., Wright, E., Swinyard, S., & de Koning, W. (2020).** Gluten-free products in the UK retail environment: Availability, pricing, and consumer opinions. International Journal of Celiac Disease, 8(3), 95-103.
- **Vriezinga, S. L., Auricchio, R., Bravi, E., Castillejo, G., Chmielewska, A., Crespo Escobar, P., Kolaček, S., Koletzko, S., Korponay-Szabo, I. R., Mummert, E., Polanco, I., Putter, H., Ribes-Koninckx, C., Shamir, R., Szajewska, H., Werkstetter, K., Greco, L., Gyimesi, J., Hartman, C., Hogen Esch, C., Hopman, E., Ivarsson, A., Koltai, T., Koning, F., Martinez-Ojinaga, E., te Marvelde, C., Mocic Pavic, A., Romanos, J., Stoopman, E., Villanacci, V., Wijmenga, C., Troncone, R., & Mearin, M. L. (2014).** Randomized feeding intervention in infants at high risk for celiac disease. The New England Journal of Medicine, 371(14), 1304-1315.
- **Wei, J. W., Wei, J. W., Jackson, C. R., Ren, B., Suriawinata, A. A., & Hassanpour, S. (2019).** Diagnosis and analysis of celiac disease and environmental enteropathy on biopsy images using deep learning approaches. Academia.edu.
- **Weil, D., Christmann, P.-Y., Sailley, N., & Thévenot, T. (2018).** Letter: Innovative use of the alfapump system to treat a small hepatocellular carcinoma. Alimentary Pharmacology & Therapeutics, 47(5), 695-696.
- **West, J., Fleming, K. M., Tata, L. J., et al. (2014).** Incidence & prevalence of coeliac disease and dermatitis herpetiformis in the UK over two decades: Population-based study. American Journal of Gastroenterology, 109(5), 757-768.
- **Wolf, R. L., Lebwohl, B., Lee, A. R., Zybert, P., Reilly, N. R., Cadenhead, J., Amengual, C., & Green, P. H. R. (2018).** Hypervigilance to a gluten-free diet and decreased quality of life in teenagers and adults with celiac disease. Digestive Diseases and Sciences, 63(12), 3134-3144.

List of attachments

استبيان حول حساسية الغلوتين

عزيزتي/عزيزي المشارك، نهدف من خلال هذا الاستبيان إلى جمع معلومات عن مرض حساسية الغلوتين بهدف تحسين فهمنا لهذا المرض ودراسة تأثيره على حياة المرضى ومعرفتهم به. نشكرك مقدمًا على تخصيص وقتك للإجابة على الأسئلة. نؤكد أن جميع الإجابات ستظل سرية وستُستخدم لأغراض البحث العلمي فقط.

الجزء الأول: المعلومات العامة

-الطول : .....

-الوزن : .....

-.العمر: .....

-الجنس_: ☐ ذكر ☐ انثى

- المستوى التعليمي: ☐ ابتدائي ☐ متوسط ☐ ثانوي ☐ جامعي ☐ غير ذلك .....

-مكان الإقامة : .....

الجزء الثاني: المعرفة بالمرض

-حسب رأيك، ما هي حساسية الغلوتين .....

-ما هو الغلوتين؟ .....

-أين يمكن أن نجد الغلوتين؟ .....

الجزء الثالث: معلومات حول المرض

-هل تعاني من مرض حساسية الغلوتين_؟ ☐ نعم ☐ لا

-ما هو العمر الذي بدأت فيه أعراض المرض؟.....

-ما هي الأعراض المباشرة التي تعاني منها؟_ (اختر كل ما ينطبق)

☐مشاكل هضمية (انتفاخ، إسهال، إمساك)

☐فقدان الوزن

☐تعب وإرهاق مستمر

☐آلام في البطن

☐مشكلات جلدية (مثل الطفح الجلدي)

☐تساقط الشعر

☐أعراض أخرى (يرجى التوضيح.).....

-أين تم تشخيص مرضك ؟

☐في عيادة طبيب عام

☐في عيادة طبيب مختص بأمراض الجهاز الهضمي

☐في مستشفى أو مركز صحي

-كيف تم تشخيص مرضك ؟

☐عن طريق تحليل الدم

☐بأخذ عينة من الأمعاء (خزعة)

☐بناءً على الأعراض التي كنت أعاني منها

-هل تعاني من أمراض أخرى_ ؟ ☐ نعم (يرجى التوضيح)..... ☐ لا

-هل هناك أحد من أفراد عائلتك مصاب بمرض حساسية الغلوتين؟_ ☐ نعم ☐ لا

- إذا نعم، من هم الأفراد المصابون بالمرض ؟_ .....

- هل ما زلت مصابًا بمرض حساسية الغلوتين ؟ - ☐ نعم - ☐ لا

- إذا كنت لم تعد مصابًا، في أي عمر اختفت الأعراض أو تحسن وضعك الصحي؟

.....

الجزء الرابع: النظام الغذائي والحياة اليومية

-ما هو نظامك الغذائي الحالي_؟ ☐ خالٍ تمامًا من الغلوتين ☐ أحيانًا أتناول أطعمة تحتوي على الغلوتين
☐ غير ملتزم بنظام غذائي محدد

-ما هي الصعوبات التي تواجهها في اتباع نظام غذائي خالٍ من الغلوتين؟_ (اختر كل ما ينطبق)
☐صعوبة العثور على المنتجات المناسبة
☐تكلفة المنتجات الخالية من الغلوتين
☐عدم الوعي الكافي بالمكونات
☐صعوبة الالتزام بالنظام الغذائي
☐غير ذلك (يرجى التوضيح).....

-ما هي المنتجات التي تستهلكها ؟
☐خبز خالي من الغلوتين
☐معجنات خالية من الغلوتين (مثل الفطائر والكعك)
☐حلويات خالية من الغلوتين (مثل البسكويت والشوكولاتة)
☐ غير ذلك (يرجى التوضيح).....

-هل تجد صعوبة في شراء هذه المنتجات_؟ ☐ متوفرة بسهولة ☐ متوسطة الصعوبة ☐ قليلة التوفر

-ما هو رأيك في الاسعار المخصصة لشراء هذه المنتجات؟ ☐ منخفضة ☐ متوسطة ☐ مرتفعة

-هل تتناول الطعام خارج المنزل؟ ☐ نعم ☐ لا

-إذا كنت تتناول الطعام خارج المنزل، هل تجد صعوبة في العثور على خيارات خالية من الغلوتين؟
☐ نعم، صعب جدًا
☐ أحيانًا يكون صعبًا
☐ لا، هناك خيارات متاحة بسهولة

-ما هي الصعوبات التي تواجهها عند تناول الطعام خارج المنزل؟ (يمكنك اختيار أكثر من إجابة)
☐ - قلة توفر الأطعمة الخالية من الغلوتين في المطاعم
☐ - ارتفاع الأسعار في المطاعم التي تقدم خيارات خالية من الغلوتين
☐ - لا أواجه أي صعوبات

الجزء الخامس: تحسين المعرفة والتوعية

-هل تعتقد أن هناك حاجة لزيادة التوعية بمرض حساسية الغلوتين_؟ ☐ نعم ☐ لا

-ما هي الطريقة الأنسب لزيادة الوعي بالمرض برأيك_؟
☐وسائل الإعلام (تلفزيون، إنترنت، صحف)
☐حملات صحية في المدارس والمستشفيات
☐دورات وندوات تعليمية
☐غير ذلك (يرجى التوضيح) .....

شكرًا لك على مشاركتك!
يرجى ملء الاستبيان بدقة وتقديم