Epidemiology of Celiac Disease

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1 Introduction

The journey of celiac disease (CD) from its first description by Samuel Gee to a great breakthrough discovery of wheat being the cause of CD, based on diligent clinical observation and clinical enquiry of five young patients, by Willem Karel Dicke has been very inspiring [1, 2]. CD is a unique in the sense that the treatment of the disease has been discovered decades before understanding or unravelling of its pathophysiology. While the introduction of gastrointestinal endoscopic techniques in 1970s for taking biopsies from the intestinal mucosa and identification of two human leukocyte antigen (HLA) molecules (HLA-DQ2 and HLA-DQ8) in late 1980s led to the understanding of the pathology and pathophysiology of CD, the discovery of serologic tests such as anti-endomysial antibody (EMA), anti-tissue transglutaminase antibody (IgA tTG Ab), or anti-deamidated gliadin peptide antibody (anti-DGP Ab) has not only allowed screening of high-risk group for CD, but also made it possible to estimate the true prevalence of CD in the general population [3–8].

While the abovementioned discoveries eased the making of a diagnosis, certain other factors in our understanding of the distribution of the disease and its clinical characteristics have led to an increase in the rate of the diagnosis of CD globally. Firstly, while CD has been thought traditionally to be a disease of children and seen

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only by paediatricians, the realization of the fact that CD is a disease of life-long, patients with CD started getting diagnosed in all age groups including adults and elderly [9–11]. Secondly, once believed to be affecting people of European origin predominantly, studies from other continents later confirmed that the CD also affects non-Caucasian population including Africans and Asians [12, 13]. Thirdly, once thought that the gluten hypersensitivity in CD is limited to the small intestinal mucosa and thus only those having gastrointestinal manifestations were screened for CD. It later became apparent that CD affects many other organs and it has a wide spectrum of clinical manifestations. Hence patients having non-gastrointestinal manifestations even in the absence of gastrointestinal symptoms started getting diagnosed as CD [14–17]. The last factor which led to an increase in the rate of diagnosis of CD is the ease of making a diagnosis by simplification of the diagnostic criteria. Prior to the revised diagnostic criteria for CD in 1990, now of a historical importance, making a diagnosis of CD required three sequential intestinal mucosal biopsies [18]. Now with further simplification of diagnostic criteria, a diagnosis of CD can be made solely on the basis of presence of high titre of anti-tTG Ab alone [19]. With advancement created by fundamental and clinical research, CD has now become the commonest autoimmune diseases of humans.

2 Origin of Epidemiology of CD

Initial epidemiological studies conducted in 1950, when the diagnosis of CD was based entirely on the presence of typical gastrointestinal symptoms, showed a cumulative prevalence of 1 in 8000 in England and 1 in 4000 in Scotland [20]. With the invention of more specific tests for malabsorption, advent of intestinal biopsy, and increase in awareness about CD, the prevalence of CD increased in 1970s to 1 in 450 in Ireland, Scotland, and Switzerland [21, 22].

3 Modern Epidemiology of CD

A multicentre study from Italy involving school children aged 6–15 years, using the three-layered strategy of clinical screening, serological tests, and intestinal biopsies gave birth to the modern epidemiology of CD. Among 17,201 healthy Italian students, the overall prevalence of CD was found to be 1 in 184. More interestingly, only 1 in 7 was previously diagnosed as CD, highlighting a big iceberg phenomenon, where clinically detectable patients were just a few and a larger number of subjects remained clinically undiagnosed [23]. This landmark serology-based study catalyzed the exploration of epidemiology of CD in different parts of the world.

3.1 The Global Perspective

A real-time assessment of the prevalence of CD is denoted via seroprevalence of CD (proportion of people having a positive anti-tTG Ab and /or anti-endomysial Ab) and prevalence of biopsy-confirmed CD (proportion of individuals with villous abnormalities of modified Marsh grade 2 or more along with a positive serological test).

3.2 Global Seroprevalence of CD

The pooled global seroprevalence of CD in the general population is 1.4% (95% CI 1·1%, 1·7%), as shown by a systematic review and meta-analysis of population-based studies, including 275,818 [13]. The seroprevalence of CD varies from continent to continent, and the highest seroprevalence has been reported in Europe and Asia (Table 1). Furthermore, the seroprevalence of CD also varies from country to country, the highest being in Algeria, Czech Republic, India, Israel, Mexico, Saudi Arabia, Sweden, Portugal, and Turkey and lowest in Estonia, Germany, Iceland, Libya, Poland, Republic of San Marino, and Spain [13] (Fig. 1).

3.3 Global Prevalence of Biopsy-Confirmed CD

The global pooled prevalence of biopsy-confirmed CD has been shown to be 0·7% (95% CI 0·5%, 0·9%) in a systematic review and meta-analysis of population-based studies [13]. On stratification of countries into quintiles based on the prevalence of biopsy-confirmed CD, countries with the highest prevalence (76–100th quintile) include Argentina, Egypt, Hungary, Finland, India, New Zealand, and Sweden and the countries with the lowest prevalence (0–25th quintile) include Brazil, Germany, Republic of San Marino, Russia and Tunisia (Fig. 2).

Table 1 Continent wise seroprevalence and prevalence of biopsy-confirmed CD disease

Continent	Seroprevalence of CD (CI)	Prevalence of Biopsy confirmed CD (CI)
Europe	1.3 (1.1–1.5)	0.8 (0.6–1.1)
North America	1.4 (0.7–2.2)	0.5
South America	1.3 (0.5–2.5)	0.4 (0.1–0.6)
Africa	1.1 (0.4–2.2)	0.5 (0.2–0.9)
Asia	1.8 (1–2.9)	0.6 (0.4–0.8)
Oceania	1.4 (1.4–1.8)	0.8 (0.2–1.7)

CD: Celiac disease; CI: Confidence interval

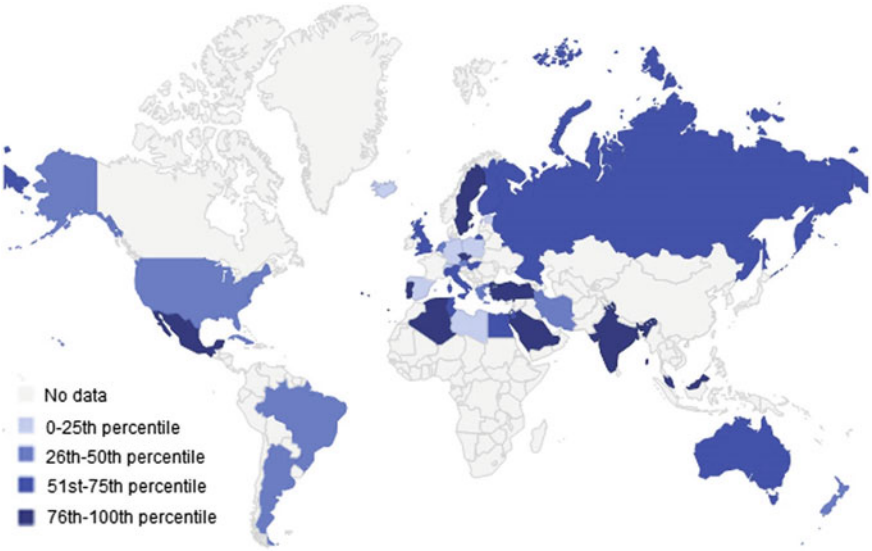

Fig. 1 Worldwide celiac disease seroprevalence rates for the countries reporting data. Prevalence values were stratified into 4 groups of percentiles representing the 0–25th percentile (light grey) to the 76–100th percentile (dark black). The lowest and highest percentiles include countries with pooled national prevalence ranging from 0.2% to 0.8% and 2.1% to 8.5%, respectively (Reprinted from the Clinical Gastroenterology and Hepatology volume 16,issue 6, June 01,2018,Singh et al., Global prevalence of celiac disease—systemic review and meta-analysis, P823-836,2021,with permission from Elsevier)

Most population-based epidemiological studies to assess the prevalence of CD are based on a positive celiac serological test, and the diagnosis of CD in all seropositive patients has not been confirmed by intestinal mucosal biopsies, which likely is the explanation of the differences in the population-based seroprevalence and prevalence of biopsy-confirmed CD [13]. Furthermore, the population-based prevalence data is still not available from many countries and thus the presently observed prevalence data may not reflect the real global prevalence of CD.

3.4 Continent-Wise Prevalence of CD

Prevalence of CD in Europe

Most of the initial studies on the prevalence of CD has risen from European countries such as Italy, UK, Finland. In the first multinational European study including Finland, Germany, Italy, and the UK, 29,212 subjects were screened for CD using anti-tTG antibody, and all those who had either a positive or a borderline titre of anti-tTG Ab were further tested for EMA in their serum. The overall

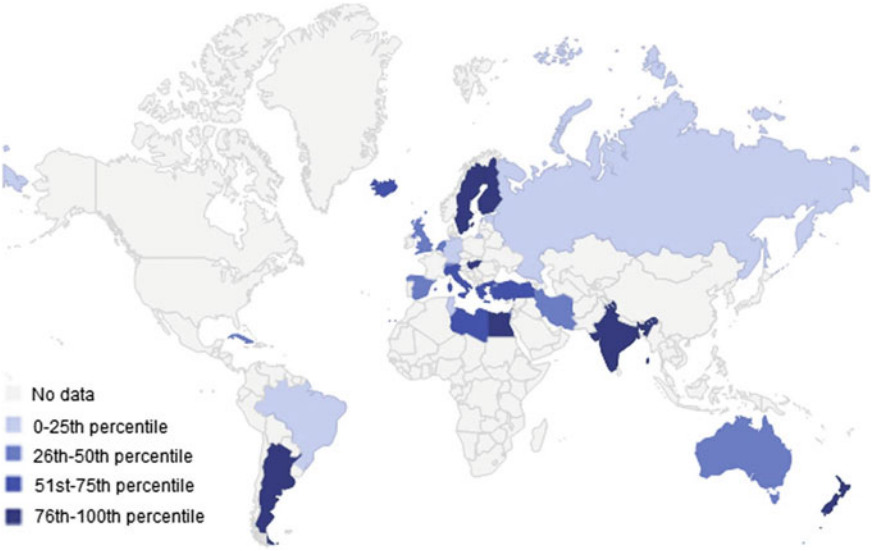

Fig. 2 Worldwide celiac disease prevalence rates (based on biopsy) for the countries reporting data. Prevalence values were stratified into 4 groups of percentiles representing the 0–25th percentile (light grey) to the 76–100th percentile (dark black). The lowest and highest percentiles include countries with a pooled national prevalence ranging from 0.2% to 0.4% and 0.9% to 2.4%, respectively. (Reprinted from the Clinical Gastroenterology and Hepatology volume 16, issue 6, June 01,2018, Singh et al., Global prevalence of celiac disease - systemic review and meta-analysis, P823-836,2021,with permission from Elsevier)

prevalence CD in this multinational European study has been reported to be 1.0% (95% CI 0.9–1.1) [24]. Interestingly, the prevalence of CD was not uniform in the four participating European countries, despite sharing of a similar distribution of causal factors (level of gluten intake and frequency of HLA-DQ2 and DQ8 genotype). The prevalence of CD was 2.0% (95% CI 2.0–2.8) in Finland, 1.5 (95% CI 1.1–1.9) in UK, 0.7% (95% CI 0.4–1.0) in Italy, and the lowest prevalence of 0.3% (95% CI 0.1–0.5) in Germany [24]. Interestingly another study later from Germany including 12,741 participants, aged 1–17 years, has shown the prevalence of CD to be 0.9%, which is much higher than that reported earlier in the multicentre European study [25].

Taken together, the seroprevalence and prevalence of biopsy-confirmed CD in Europe has been reported to be 1.3% (95% 1.1–1.5) and 0.8% (95% 0.6–1.1), respectively in a systemic review and meta-analysis of 33 studies conducted in 2018 [13]. While the abovementioned systematic review has included studies including both adults and children, the systematic review and meta-analysis in 2021 has focused on the prevalence of biopsy-confirmed CD in children in Europe. The prevalence of biopsy-confirmed CD in children in Europe in this study has been reported to be 0.7%, but varying widely between 0.10 and 3.03%. Furthermore, a regional variation was noted in the prevalence of CD in children and the prevalence

is reported to be significantly higher in northern Europe (1.6%) than that in eastern (0.98%), southern (0.69%), and western (0.60%) Europe [26].

Prevalence of CD in America (North America and South America)

While CD has been considered to be an uncommon disease in America in earlier decades, a population based prevalence study in 2003 reported that 1 in 133 Americans having CD [27]. Similarly in other study it was 1 in 141 [28]. Taken together, a systematic review and meta-analysis of population-based seven studies including 17,778 subjects revealed that the prevalence of CD, based on a positive serological test, in North America is 1.4% (95% CI 0.7–2.2) [13].

CD is well-known in those South American countries that are populated by individuals of European origin, such as Brazil. In a study including 4405 subjects from Brazil, the overall seroprevalence and prevalence of biopsy-confirmed CD has been reported to be 3.6 and 3.4 per 1000, respectively. Prevalence of CD in adults and children has been reported to be 2.1 and 5.4 per 1000, respectively [29]. As per a systematic review of the studies from South America, the pooled seroprevalence and prevalence of biopsy-confirmed CD was 1.3% (95% 0.5–2.5) (11 studies and 20,245 subjects screened) and 0.4% (0.1–0.6) (5 studies and 16,550 subjects), respectively [13].

Prevalence of CD in Oceania

As in the European countries, a population-based study from Australia including 3011 subjects showed the seroprevalence and prevalence of biopsy-confirmed CD to be 1 in 251 and 1 in 430, respectively [30]. A similar population-based study from New Zealand including 1064 subjects has shown the prevalence of CD to be 1.1% [31].

Prevalence of CD in Africa

The pooled seroprevalence (7 studies and 15,775 subjects) and prevalence of biopsy-confirmed CD (4 studies and 7902 subjects) in African continent has been shown to be 1.1% (95% CI 0.4–2.2) and 0.5% (95% CI 0.2–0.9), respectively [13]. The Saharawi population of Arab-Berber origin, originally living in western Sahara, has the highest prevalence of CD in the world. A study of 990 Saharawi children showed that the prevalence of CD in this population is 5.6% [32]. Specifically in other regions of Africa, the prevalence of CD has been reported to be 0.5% in Egypt [33], 0.8% in Libya [34] and 0.6% in Tunisia [35].

Prevalence of CD in Asia

Until recent times, CD was considered to be a rare disease in Asia and patients presenting with diarrhoea and malabsorption were diagnosed usually as having tropical sprue [36]. After the widespread availability of serological tests, multiple screening studies have been performed in many Asian countries such as Turkey, Iran, Israel, Jordan, and India and almost all of them summarily show that CD is not an uncommon and it most often remains underdiagnosed in Asia [37]. Due to the

heterogeneity of the population, genetics, economic conditions, and the dietary habits, the epidemiology of CD is different in different parts of Asia.

In India, CD has been recognized mainly in the northern part of India, where wheat is the predominant cereal consumed and a population-based study including 2879 subjects showed a prevalence of CD to be 1.04% (1 in 96) [38]. Later, a pan-India study including 23,331 healthy adults from three different regions of India, showed a regional variation in the prevalence of CD. While the age-adjusted seroprevalence of CD in Northern, North-Eastern regions were 1.23%, 0.87%, respectively, it was only 0.10% in the Southern region, showing Northern and Southern region gradients in the prevalence of CD [39].

The epidemiology of CD in China, the largest country, was largely unknown until recent years, except for a small case series. In a cross-sectional study including 19,778 Chinese adolescents and young adults (age 16–25 years) from 27 geographic regions in China showed that more than 2% (2.19%) of them had at least one of the serological test positive including 1.8% for IgG anti-DGP Ab and 0.36% for IgA anti-tTG Ab [40]. The prevalence of people with a positive antibody varied remarkably among different regions of China and it was 12 times higher in the Northern provinces, such as Shandong, Shaanxi, and Henan, where wheat was the staple diet [40]. In another recent study, including 2277 inpatients with gastrointestinal symptoms in four major ethnic groups of Xinjiang Uyghur Autonomous Region of China, the seroprevalence and prevalence of biopsy-confirmed CD was observed to be 1.27% (95% CI, 0.81–1.73%), and 0.35% (95% Cl, 0.11–0.59%), respectively [41]. Interestingly, among 246 patients with diarrhoea-predominant irritable bowel syndrome in China, 2.85% were reported to have CD [42]. These preliminary studies have established the foundation for the exploration of the exact prevalence of CD and regional geographical differences in the prevalence of CD in China.

In a pilot study, including 562 young healthy volunteers from Malaysia, the seroprevalence of CD has been reported to be 1.25% (95% CI 0.78–1.72%) [43]. In a study from Japan including 2008 subjects, anti-tTG Ab was found to be positive in a high proportion (8%), however, none of them was EMA positive and only one showed celiac-type alterations at the small intestinal biopsy [44]. Similarly, in a study including 1961 Vietnamese children, the seroprevalence, based on anti-tTG Ab, was observed to be 1%, but none of them was positive for EMA [45].

Summarizing the prevalence studies addressing low-risk groups from Asian Pacific region, a recent systemic review and meta-analysis has shown that the pooled sero-prevalence of CD among low-risk groups is 1.2% and that of biopsy-confirmed CD is 0.61% [46]. Furthermore, the authors also segregated and reported the prevalence of CD in the middle east (Iran, Turkey, Saudi Arabia, Israel, Jordan), south-east Asia (India, Malaysia, and Egypt) and Eastern Asia. The pooled seroprevalence and prevalence of biopsy-confirmed CD in the Middle East region and South-East region of Asia are 1.6% (95% CI 1.2–2.1) and 0.6% (95% CI 0.4–0.8); and 2.6% (95% CI 0.3–7.2) and 0.8% (0.4–1.4), respectively, which are quite similar to that reported from many European countries. Interestingly, the seroprevalence of CD is found to be lowest (0.06%; 95% CI 0.03–0.09%) in the East-Asian countries [46].

3.5 Prevalence of CD Over Time

Looking at the time trends of the prevalence of CD, a systematic review and meta-analysis stratified studies reporting prevalence of CD into two time periods: January 1991 to December 2000 and January 2001 onward. The result of the systematic review shows that the prevalence of CD has increased over time from 0.6% in 1991 to 2000 to 0.8% between 2001 and 2016 [13].

4 Variations in the Prevalence of CD as Per Age, Gender, Geographical Distribution

4.1 Children Versus Adults

While CD was described originally in paediatric patients and believed to be a disease of children only, over time but it has been realized that CD can be diagnosed at any age group including elderly [13]. A systematic review including 43 studies has reported the prevalence of biopsy-confirmed CD in the paediatric and adult patients. The pooled prevalence of biopsy- confirmed CD is higher in children in comparison to that in adults (0.9% vs. 0.5%). While the prevalence of CD is higher in children, the absolute number of patients with CD globally and in each country, is likely to be higher in the adult age-group because of much higher proportion of adults in any country compared to children in that country [13].

4.2 Men Versus Women

As with many other autoimmune diseases, CD is more common in women as compared to men. A systematic review and meta-analysis has also confirmed that the pooled prevalence of biopsy-confirmed CD higher in women (0.6%; 95% CI, 0.5%–0.8%) in comparison to that in men (0.4%, 95% CI, 0.3%–0.5%) [13].

4.3 Geographical Location

A higher prevalence of many autoimmune diseases such as multiple sclerosis, rheumatoid arthritis and inflammatory bowel disease has been reported at higher geographical latitudes [47–49]. The associations between the autoimmune diseases and the latitude has been linked to less solar exposure and resultant vitamin D deficiency in them. In a systematic review involving 128 studies, with 155 prevalence estimates representing 40 countries, the prevalence of CD has been

reported to be higher at higher latitudes of 51 to 60° (relative risk of 1.62) and 61 to 70° (relative risk 2.30), in comparison to prevalence at latitudes of 41 to 50° as reference level [50]. In this study, when latitudes were categorized into intervals of 10° latitudinal increments, the prevalence of CD increased incrementally at latitude higher than 40°.

5 Incidence of CD

The incidence of CD is expressed as a rate, i.e. the number of new clinically diagnosed patients with CD per 100,000 subjects over one year. Due to the diffusion of CD serological tests in clinical practice and the improved awareness about the clinical polymorphism of CD, CD incidence has greatly increased in many western countries during the last decades [51, 52]. For instance, during 2010–2014, twenty times more patients were diagnosed in UK than that during 1975–1979 [53]. In the US (Olmsted County, Minnesota) the overall age and sex-adjusted incidence of CD increased from 11.1 per 100,000 persons/year in 2000–2001 to 17.3 in 2008–2010 [54].

While there is paucity of population-based study for incidence from many parts of the world except industrialized and developed countries, in a recent systematic review and meta-analysis, King et al. reported the differences in incidence of CD before the year 2000 and that after year 2000. The pooled average annual incidence of CD has been estimated to be rising by 7.5% (95% CI: 5.8, 9.3) per year over the past several decades [55]. The systematic review showed that the pooled incidence of CD in women and men is 17.4 (95% CI: 13.7, 21.1) and 7.8 (95% CI: 6.3, 9.2) per 100,000 person-years, respectively. Children specific incidence of CD is higher (21.3 per 100,000 person-years) in comparison to that of the adults (12.9 per 100,000 person-years) [55].

Another systematic review and meta-analysis of incidence of CD in children in Europe showed a large increase in the incidence of diagnosed CD across Europe and it has reached 50 per 100 000 person-years in Scandinavia, Finland, and Spain [26]. The median age at diagnosis of CD has increased from 1.9 years before 1990 to 7.6 years since 2000.

As discussed above, while the incidence rates for CD are increasing in many countries such as UK [53], USA [56], and New Zealand [57], the incidence rate in Finland and Sweden has reached peaked and it is stabilizing [58, 59]. This increase in incidence of CD is not likely only due to improvement in the rate of diagnosis because of ease of diagnosis and increase in the awareness of the disease amongst physicians but also due to changes in our environment and eating practices [60, 61].

6 Risk Factors for CD

CD occurs because of interaction between both environmental (gluten) and genetic factors (HLA and non-HLA genes), and the distribution of these two components can guide to identify the areas of the world at risk for CD [62].

7 Wheat, Barley, and Rye

During the very early part of the evolution, men led a nomadic life and obtained food by hunting, fishing and collecting fruits and vegetables. Therefore, we can infer that CD did not exist during the Palaeolithic age, as the diet of hunter-gatherers consisted of only meat, vegetables, seeds and fruits and was gluten-free by its origin. About 10,000 years ago in a small region of South-Western Asia, called the "Fertile Crescent" including Southern Turkey, Lebanon, Syria, Palestine and Iraq, the local community started cultivating wild grains due to the special environmental conditions created by the flooding. In the Fertile Crescent, some tribes changed their lifestyle from nomadic to a stable settlement because land cultivation permitted them to store food [63]. The first wheat varieties, which were successfully domesticated, were Einkorn (diploid wheat) and Emmer wheat (tetraploid wheat) [64]. The progressive spread of agriculture to Europe took place through the migration of farmers and their mixing with and partially replacing the indigenous European population. The agricultural spread was stimulated by population growth (as a result of the increasing availability of food) and local migratory activity [33, 65, 66].

In the evolutionary process, the genome of wheat has changed from diploid (14 chromosomes) to hexaploid genome (42 chromosomes) [67]. The genome of the most ancient wheat is diploid and is called AA, BB, DD. These grass-like wheat species had a very low seed yield and their seed dropped easily. Natural hybridization between two of these diploid species led to birth of the tetraploid *Triticum* species having AABB genome. Finally, around 4000 BC, natural hybridization *T. turgidum* (dicoccum) carrying the AABB genome and a wild diploid species *Aegilops tauschii* carrying the D genome led to origin of Bread wheat (*Triticum aestivum*). The introduction of the D genome in the wheat improved the bread-making properties of the wheat [68, 69].

The protein content of wheat grain varies between 8 and 17% of its total mass. Gluten comprises of 78–85% of the total wheat endosperm protein. Gluten proteins can be divided into two main fractions according to their solubility in aqueous alcohols: the soluble gliadins and the insoluble glutenins. Gliadins are mainly monomeric proteins with molecular weights (MWs) around 28,000–55,000 and can be classified according to their different primary structures into the *a*-, *b*-, *g*- and *w*-type. Glutenin consists of glutenin subunits of high (MW 67,000–88,000) or low MW (MW 32,000–35,000) that are connected by intermolecular SS bonds.

Noncovalent bonds such as hydrogen bonds, ionic bonds and hydrophobic bonds are important for the aggregation of gliadins and glutenins and implicate structure and physical properties of dough. Glutenins confer elasticity, while gliadins mainly confer viscous flow and extensibility to the gluten complex. Thus, gluten is responsible for most of the viscoelastic properties of wheat flour dough, and it is the main factor dictating the use of a wheat variety in bread and pasta making.

Gliadins and glutenins have a unique amino acid composition with a high content of proline (15%) and glutamine (35%). Moreover, they contain domains with numerous repetitive sequences rich in these amino acids. The incomplete digestion of gliadin by digestive tract enzymes leads to the generation of peptides, many of which are immunogenic for patients with CD [64, 70]

Over the past five decades, several changes in the pattern of wheat consumption have been observed including an increase in per capita consumption of wheat, an increase in the use of gluten in food processing and an increase in the consumption of processed foods. Furthermore, an increase in CD-related T-cell stimulatory epitopes has also been observed in wheat. It is conceivable that these changes in the wheat consumption pattern and increase in T-cells stimulatory epitopes in wheat may be the reasons for an increase in the incidence of CD world over [71].

7.1 Genetic Risk Factors

CD is considered to be a polygenic disease with a complex non-Mendelian pattern of inheritance, involving both MHC and non-MHC genes. The strong genetic predisposition is demonstrated by concordance rate of 80% in monozygotic twins and 20% in dizygotic twins [72, 73]. Furthermore, the prevalence of CD in the first-degree relatives of patients with CD has been reported to vary from 1.6 to 38% [74–76]. A systematic review and meta-analysis have shown that 7.5% of first-degree relatives and 2.3% of second-degree relatives have CD. The risk of CD is 1 in 7 in sisters,1 in 8 in daughters, 1 in 13 in sons, 1 in 16 in brothers, 1 in 32 in mothers, and 1 in 33 in fathers [77].

CD is a multigenic disorder, in which the most dominant genetic risk factors are the genotypes encoding the HLA class II molecules HLA-DQ2 (encoded by HLA-DQA1*0501 and HLA-DQB1*02) and HLA-DQ8 (encoded by HLA-DQA1*0301 and HLA-DQB1*0302) [78, 79]. About 90–95% of individuals with CD carry the HLA-DQ2 heterodimer encoded either in cis or in trans, and HLA-DQ8 [80, 81]. Approximately 20–30% of the general population of Europe, America, Australasia certain part of Asia also carry HLA-DQ2 or DQ8 haplotype [82]. Interestingly, this most of these people do not develop CeD even if they consume gluten.

While ingestion of gluten and HLA-DQ2 or HLA-DQ8 are essential factors, there however are many other factors which likely play a role in the development of CD. Currently, 57 susceptibility loci, not related to HLA, have also been identified by genome-wide association studies, each of which is estimated to be associated with small risk of developing CD [83].

Table 2 Risk factor for celiac disease

Essential factors	Risk factor modifier
Gluten	Amount of gluten ingestion Timing of gluten introduction during weaning Gluten processing
Genetic MHC gene: HLA-DQ2, HLA-DQ8	Non MHC genes Epigenetic factor
	Breastfeeding Childhood infection, Use of antibiotics in childhood Socioeconomic status

The relevance of HLA and other relevant environmental factors such as age of the introduction and amount of gluten, infant feeding, infection in childhood, antibiotics use in childhood and socioeconomic factors that play a relevant role in the epidemiology of CD and are addressed in detail in other part of this book (Table 2).

8 Conclusions

While CD is now a global disease, and approximately 40–60 million people around the world are estimated to have CD. Of them only a proportion of patients are diagnosed, and a majority still remains undetected. There is a need to increase the awareness of CD amongst the general population and the physicians.

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