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Prevalence of Celiac disease among siblings of Celiac disease patients

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ABSTRACT

Aim: To determine the prevalence of celiac disease in siblings of patients.
Several studies have reported that celiac disease is more common in family members of patients with this disease than in the healthy population. In the first degree relatives of patients the prevalence rate of celiac disease reaches 10 to 20 %. The Inheritance of CD appears to be polygenic with a very high heritability, or a dominant inheritance with a very low rate of expression in hetero zygotes. Thus relatives of celiac patients, especially first degree relatives are at high risk of developing celiac disease. Gastroenterologists and practitioners should ask about family history of celiac disease among their patient's parents, siblings and children. And if they are present during the clinic visit, they should offer screening.

Key Words : Celiac Disease, Gluten sensitivity, First degree relatives, Prevalence, Autoimmune disorder, Genetic disorder

INTRODUCTION

Celiac disease is one of the most common genetic disorders, affecting approximately 1 % of individuals worldwide. In predisposed individuals, gluten ingestion precipitates chronic autoimmune responses that can manifest in a variety of ways and affect multiple organ systems. In part, the incidence of celiac disease has risen because of improved awareness of the disease and more accurate and less invasive diagnostic testing. According to experts at All India institute of medical sciences, celiac disease affects close to six to eight million people in India. Celiac disease must not be confused with gluten allergy or its intolerance. The condition is the one where gluten consumption may cause damage to the small intestine.

Celiac disease is a serious autoimmune disease that occurs in genetically predisposed people where the ingestion of gluten leads to damage in the small intestine. It is estimated to affect 1 in 100 people worldwide. Two and one- half million Americans are undiagnosed and are at risk for long term health complications. When people with celiac disease eat gluten (a

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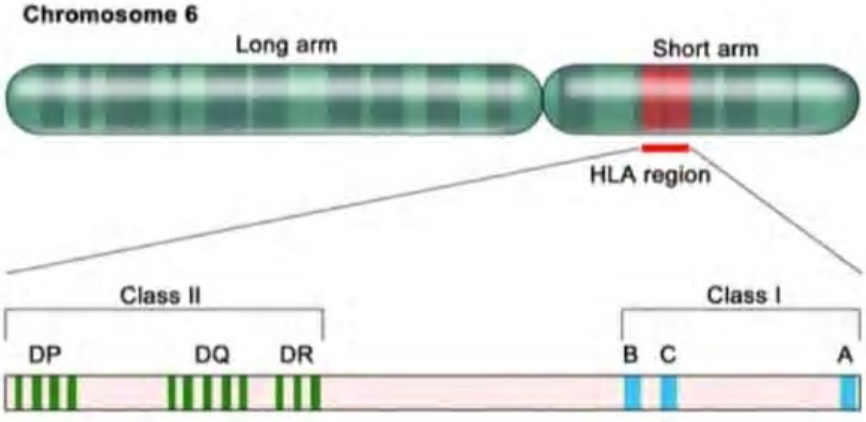
protein found in wheat, rye and barley), their body mounts an immune response that attacks the small intestine. These attacks lead to damage on the villi, small finger like projections that line the small intestine, that promote nutrient absorption. When the villi get damaged, nutrients can not be absorbed properly into the body.

Researches revealed that celiac disease more common in one ethnicity. Clinical findings shows that celiac disease was most common among US residents of South Indian, East Asians and Hispanic ancestry. The rate of celiac disease among patients of Jewish and middle Eastern ethnicities was similar to that of other Americans (1). Today, it's estimated that about one in 100 people have Celiac disease. Doctors don't know why celiac is on rise. It may be due to changes in the way wheat is grown and processed, or the ubiquity of gluten in medications and processed foods. The highest prevalence of celiac disease is in Ireland and Finland and in places to which Europeans emigrated, notably North America and Australia. In these Populations, celiac disease affects approximately 1 in 100 individuals. It is widely accepted that celiac disease is a global public health concern. In America The overall prevalence of this condition is 1.4% on the basis of serological findings and 0.7 % on the basis of biopsy findings (2). However, specific national population based prevalence studies are needed because the prevalence of celiac disease varies with factors such as sex, age and location. Approximately 3 million people in Europe and another 3 million people in the united states, and 6 to 8 million in India are estimated to be affected by celiac disease. Celiac disease is prevalent in European countries with temperate climates. The incidence of celiac disease is increasing among certain populations in Africa (Saharawui population), Asia (India) and the Middle East (3,4).

Several studies have reported that Celiac disease is more common in family members



Human chromosome 6 with amplification of the human lymphocyte antigen (HLA) region. The locations of specific HLA loci for the class I B, C and A alleles and the class II DP, DQ, and DR alleles are shown.

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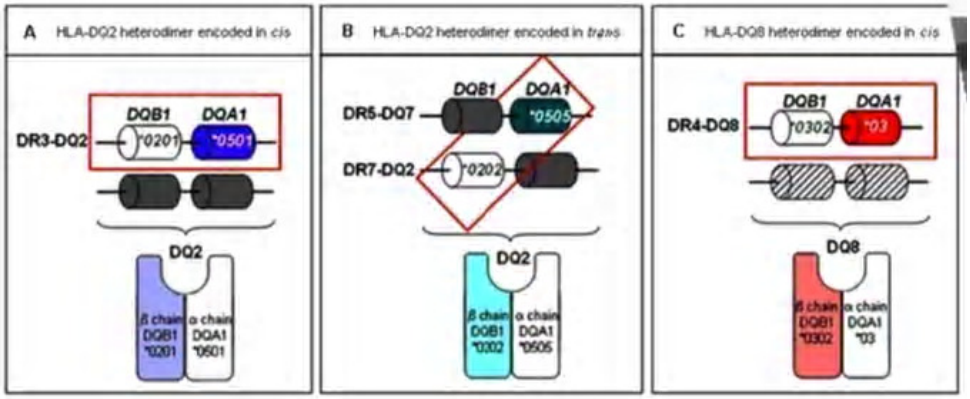
HLA - DQA1 and HLA-DQB1 heterodimers



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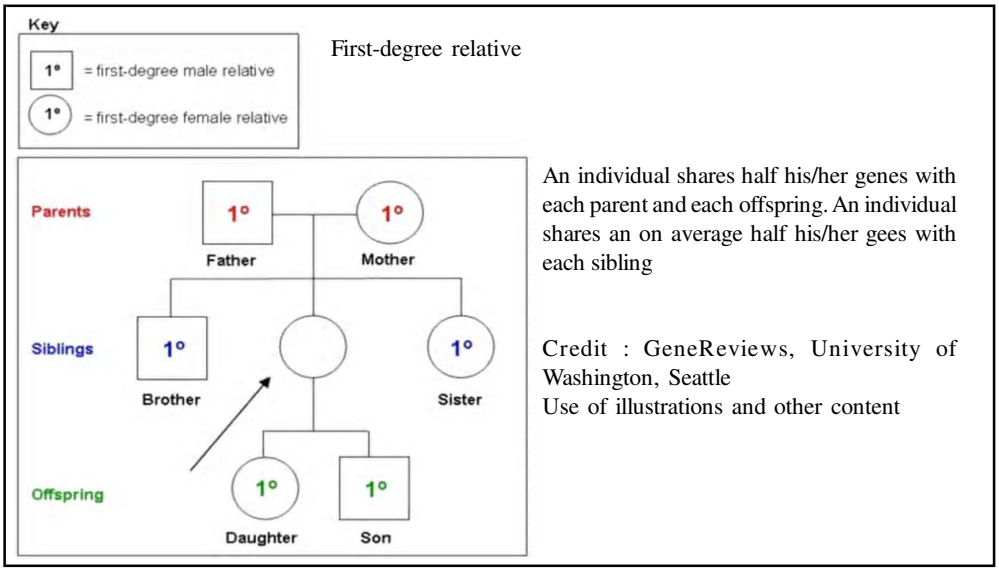
of patients with this disease than in the healthy Population. In the first degree relatives of patients, the prevalence rate of CD reaches 10 to 20 %. The inheritance of CD appears to be polygenic with a very high heritability, or a dominant inheritance with a very low rate of expression in heterozygotes. The concordance rate of CD among HLA- identical siblings is approximately 30 % , mapping a great part of the genetic susceptibility to CD to the HLA region on chromosome 6. Evidence from different populations suggests that primary association of CD is with DQa / b heterodimer encoded by the DQA1*0501 and the DQB1*0201 genes. Predisposition to CD has been mapped to HLA DQ2, which appears to a dominant gene and to HLA DQ8.

No susceptibility genes other than HLA DQ have been yet identified (5). Studies revealed that celiac disease, a complex and serious autoimmune disorder, tends to run in families. And



An individual shares half his/her genes with each parent and each offspring. An individual shares an on average half his/her gees with each sibling

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people with a relative – specially a parent, sibling or child – who has celiac disease are at an elevated risk of developing the disease themselves. They might not have the classic symptoms associated with it, or even have any symptoms at all. The two genes most closely linked to celiac disease are HLA - DQ2 and HLA - DQ8. Nearly everyone who is diagnosed with celiac disease carries at least one if these two genes that they inherited from their mother or father. Among the world's population, HLA typing is present in 98.6 % of patients with CD, with a high negative predictive value. Moreover, in the general population who do not have the diagnosis of CD, HLA- DQ2 and / or HLA - DQ8 is present in approximately 40 % of the population, and this percentage increases among patients who are not celiac but has first degree relatives with celiac disease. It is worth remembering that HLA is a genetic trait, and therefore its presence in the general population has a higher prevalence in relatives of celiac patients. The closer are the relatives, more prevalent may be antigen histocompatibility (6).

Table 1 : High risk populations for celiac disease
Relatives, especially first-degree
Anemia, especially iron deficiency
Osteopenic bone disease
Insulin-dependent diabetes (type 1), especially children
Liver disorders, especially AIH and PBC
Genetic disorders, including Down and Tumer's syndrome
Autoimmune endocrinopathy, especially thyroid disease
Skin disorders, particularly dermatitis herpetiformis
Neurological disorders, including ataxia, seizures, MG
Others, including IgA nephropathy
AIR: Autoimmune hepatitis; PBC : Primary biliary cirrhosis; MG : Myasthenia gravis

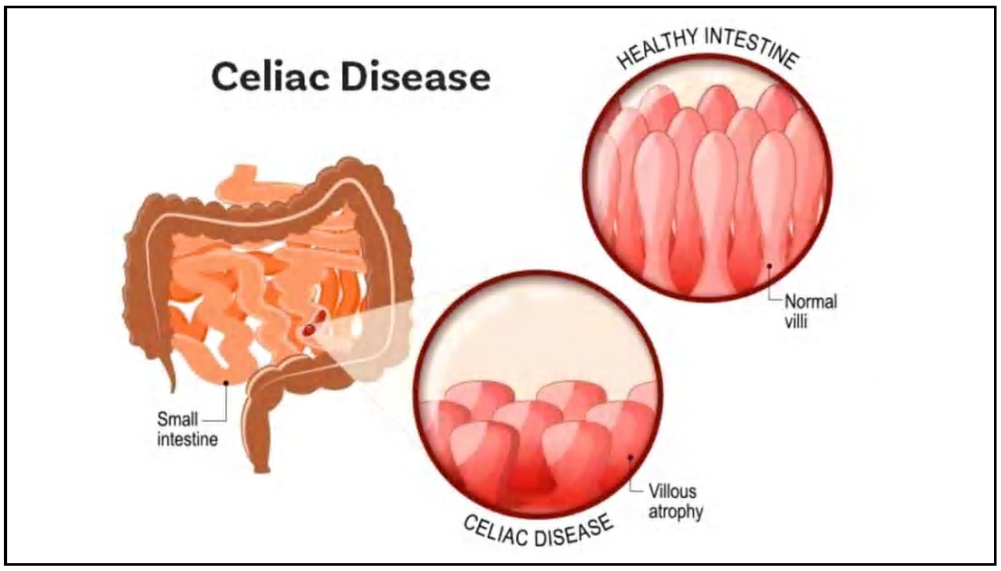
As much as one- third of the US population that does not have celiac disease also carries one of the genes. So while they are a risk factor for the disease, they not dictate that a person will develop the condition. According to National institute of health, USA, first degree relatives of someone with celiac disease have a 4 to 15 % chance of developing the condition. The risk is lower when it's a second- degree relative who has the condition, but it's still slightly higher than the risk for the general population. Celiac disease tends to cluster in families. Parents, siblings or children (first degree relatives) of people with

Table 2 : Evidence of familial risk
Biopsy and serological studies
Irish Setter dog model studies
Functional permeability studies
HLA marker studies
Genome wide expression/linkage studies
HLA : Human leukocyte antigen

celiac disease have between 4 and 15 percent chance of developing the disorder. However, the inheritance pattern is unknown.

Silent Celiac disease:

Some people have silent celiac disease, in which they have no symptoms of the disease. However, people with silent celiac disease do have immune proteins in their blood (antibodies) that are common in celiac disease. They also have inflammatory damage to their small intestine that can be detected with a biopsy (18).



In a small number of cases, celiac disease does not improve with a gluten free diet and progresses to a condition called refractory sprue. Refractory sprue is characterized by chronic inflammation of the gastrointestinal tract, poor absorption of nutrients, and an increased risk of developing a type of cancer of the immune cells called T- cell Lymphoma (19). Recent studies shows that Silent celiac disease is frequent in the siblings of newly diagnosed patients. Celiac disease is caused by environmental and genetic factors, and the relatives of celiac patients are at higher risk of developing celiac disease than the general population. This prospective study evaluates the prevalence of celiac disease in the asymptomatic siblings of celiac patients. According to researchers, Silent celiac disease is 24 –48 times more frequent in the siblings of celiac patients than in the general population. No predictive factors for sibling involvement were found. Adult females seem to tolerate less gluten than adult males (24).

Risk Estimates:

In recent years, changes have occurred with an estimate of overall prevalence rates increased in most countries, often in the region of about 1 to 2% .(7) Interestingly, in a longitudinally based study from Olmsted county in the united states over many decades, increased detection has been reported, in part, due to increased use of serological screening

(8). Recently, a report from Hangzhou in China has also suggested that the prevalence of adult celiac disease may be more common in China than previously appreciated (9). Of note, celiac disease has also been reported in immigrants to Canada from China, Japan and south Asia, particularly from the Punjab region of India (10). Even in the united states, celiac disease is now generally believed to affect 1 to 4% of general population.

High Risk groups:

Studies revealed that, there are also some high risk groups within the general celiac population, often without typical clinical symptoms, such as diarrhoea or weight loss, that may have even higher prevalence rates. Among these factors that specifically denote a higher risk for celiac disease, the single most important is a familial history of biopsy – defined celiac disease with some estimates up to 20 % or more of first degree relatives. Diagnosis of celiac disease in all of these high risk groups, however, is especially important since failure to detect celiac disease coupled with failure to treat the disease may lead to an increased risk of morality from celiac disease (11).

Familial Risk factors:

Early family studies using small intestinal biopsies have provided strong evidence for the familial nature of Celiac disease. A systematic review of these earlier studies concluded that up to 20% of first degree relatives of European descent may be at risk for celiac disease (12). Similar results have been reported from non – European populations, including a Research reporter from the Punjab region of India (13). In addition, another biopsydefinedceliacdisease have further confirmedthese findings, particularly in "at – risk"First- degree (1:22) and second – degree relatives (1:39), compare to a control "not – at – risk" group (1:133) (14). The risk appeared to be especially increased in families with at least 2 siblings diagnosed as celiac disease (15), and in this setting, more males were detected compare to females (16). Particularly significant predictors of familial risk include carrying HLA- DQ2 and being a sibling of the patients (17). Thus celiac disease is hereditary, meaning that it runs in families. People with a first degree relative with celiac disease (parent, child, siblings) have a 1 in 10 risk of developing celiac disease. Celiac disease can develop at any age after people start eating foods or medicines that contain gluten. Left untreated, celiac disease can lead to additional serious health problems (20). 2012 research study : "Prevalence of celiac disease among first degree relatives of patients with celiac disease" shows that celiac patients first degree relatives are more at risk of acquiring the disease. The objective of the thisstudy was consequently to determine the prevalence of celiac disease in a group of first degree relatives of patients with celiac disease. This study identified 23 undiagnosed cases of celiac disease among 484 first degree relatives of 195 patients with celiac disease, confirmed the high prevalence (4.8 %) of the disease in this specific group (21). In Another study: "HLA profile of celiac disease among first degree relatives from a tertiary care centre in North India" revealed that the prevalence of celiac disease among first degree relatives is 9 fold higher than the general population. High prevalence of celiac disease in presence of anaemia and short stature in seropositive First degree relatives in index study indicates need of targeted screening of this subgroup for the presence of celiac disease. Celiac disease is unlikely in the

absence of HLADQ2 /DQ8.(22)2015 study in India revealed that first degree relatives of patients with celiac disease were at risk for celiac disease and prevalence among them varies from 1.6 to 38 %. The risk of having celiac disease among first degree relatives is sister, brother, mother, father, son or daughter of index patient with celiac disease is not known. Pooled prevalence of celiac disease among first degree relatives varies considerably with their relationship with the index patient. The risk of celiac disease in first degree relatives also varies according to gender and geographical location (23). At Rochester, Minnesota, a retrospective cohort study of patients with celiac disease has found a high prevalence of the celiac disease among parents, siblings and children (first degree relatives) of the patient. The study, published in the Mayo clinic proceedings, calls for screening of all the first degree relatives of patients including those who do not show any symptoms. Worldwide, about 1% of the population is estimated to suffer from it. Celiac disease is suspected to be more prevalent in North India as wheat forms the main staple food here. The diagnosis rate of celiac disease is as low as 5% in India. The researchers studied 104 patients with celiac disease and their first degree relatives. The data was collected from electronic records from December 1983, to may 2017. The retrospective study, to be published in Mayo clinic proceedings in September, found that 44% of screened first degree relatives had celiac disease. Of those patients, 94% had symptoms that were not classic or had no symptoms at all (25).

Conclusion:

Studies have found that relatives of celiac patients, especially first degree relatives are at high risk of developing celiac disease. In view of the relatively low incidence further studies are needed to try to establish a useful and cost effective algorithm for follow up of relatives of celiac patients. Gastroenterologists and general practitioner should ask about any family history of celiac disease among their patients' parents, siblings ,and children. And if they are present during the clinic visit, they should offer screening.

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