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A STATISTICAL STUDY OF THE PREVALENCE OF CELIAC DISEASE IN ADULTS IN TWO SYRIAN GOVERNORATES (HOMS- TARTOUS) DURING THE PERIOD OF 2014-2022

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Keywords:

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ABSTRACT: Celiac disease is a multisystem immune based disorder that is triggered by the ingestion of gluten in genetically susceptible individuals. Our study was limited to a survey of the prevalence of Celiac disease in adult in two Syrian governorates (Homs and Tartous), Statistics were collected from hospitals and clinics of gastroenterologists and nutritionists, during the period of 2014-2022. 4000 cases of Celiac disease were recorded in these two Syrian governorates with a population of about 5 million people with ages ranging from 20-33, that is 0.08% in these cases. The presence of HLA class II antigens was observed in all people with Celiac disease as HLA DQ2 was found in 82% of celiac disease patients, and HLA DQ8 was found in the rest. It is very important that follow-up showed that the results of antibody tests (Transglutaminase IgA) in patients adhering to the gluten-free diet decreased from 200 to 100 "during a year of treatment" and to 20 "during two years of treatment" in all patients. The decrease in antibodies was accompanied by a clear improvement in the absorption of iron and other elements, and a good improvement in the growth of intestinal villi in patients who underwent intestinal biopsies. In the absence of Celiac disease many people identifying themselves as "being gluten sensitive". The biological basis of gluten induced symptoms in the absence of Celiac disease is largely unknown but may be related to immune responses to components of wheat apart from gluten.

INTRODUCTION: Celiac disease, also known as Celiac sprue or gluten sensitive enteropathy, is an autoimmune disorder characterized by an adverse reaction to gluten [1, 2]. Celiac disease is an immune mediated inflammatory disease of the small intestine seen in genetically predisposed individuals and is caused by sensitivity to prolamins, like wheat (gliadin), Barley (hordein), rye (secalin) and oats (avenin) [3].

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The immune reaction in Celiac disease occurs when the immune system mistakenly identifies gluten as threat and produces antibodies to attack it [2], these antibodies cause inflammation and damage to the villi, which are tiny finger-like projections in the small intestine that play a crucial role in nutrient absorption [2].

It must be pointed out from the beginning that there is a big difference between the concept of cases of maldigestion and their general symptoms and cases of malabsorption [4, 5, 6]. The former results from a functional defect resulting from a deficiency in the secretion of some yeasts belonging either to the stomach, the pancreas, liver, or intestines [7]. As for malabsorption: it is a group of diseases that

particularly affect the small intestine with significant destruction of its parietal tissue.

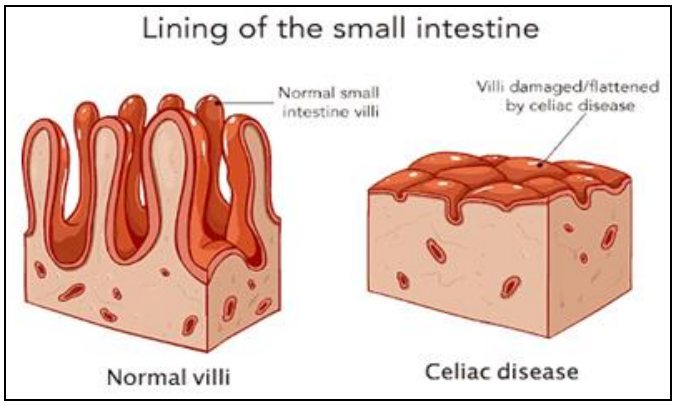

FIG. 1: THE NORMAL INTESTINE VILLI AND VILLI DAMAGED BY CELIAC DISEASE [1]

Pathophysiology: This disease is characterized by the following:

Poor absorption of nutrients from the affected section of the small intestine [9], Non-specific descriptive lesion of the intestinal mucosa [8, 9], Immediate clinical improvement following withdrawal of certain types of grains from the diet [8, 9].

Causal Pathogenic Mechanism and Pathological Anatomy: The pathogenic mechanism is explained by the presence of damage to the mucosa of the small intestine caused by a protein that is not soluble in water and soluble in alcohol known as gluten [10]. This gluten and the molecules resulting from it that cause damage differ according to the type of grains used in food as follows:

1. Loss of the normal villous structure (shortness or absence of villi), which makes the surface of the intestine flat and reduces the absorption surface [11].
2. Crypts elongate due to excessive production of undifferentiated cells, As a result of the elongation of the crypts. the total thickness of the mucosa is slightly less than that of normal mucosa [11, 12].
3. Infiltration of the lamina propria by mainly plasma and lymphocytes, and polynucleates, eosinophils, and basophils to a lesser extent.
4. Cells become cubic or flat instead of cylindrical [11, 12, 13].

Michael Marsh 1992 introduced the classification system to describe the stages of damage in the small intestine as seen under a microscope, also known as histological changes. Originally the Marsh Types ranged from 0 to 4, with a type of 3 indicating Celiac disease [14].

TABLE 1: HISTOPATHOLOGICAL DIFERENTAL DIAGNOSIS OF GLUTEN-SENSITVE ENTEROPATHY [14]

Intraepithelial lymphocytosis (Type 1)	Atrophy (Types 2 and 3)
Gastroduodenitis	Microvillus inclusion disease
Hypersensitivity to food	Autoimmune enteropathy
Infections (viral, parasitic, bacterial)	Tropical sprue
Bacterial overgrowth	Collagenous sprue
Pharmacological drugs (mainly NSAIDS)	Refractory celiac disease (including enteropathy associated T cell lymphoma)
IgA deficit	Ledions due irradiation and/or chemotherapy
Common variable immunodeficiency	Graft vs host disease
Crohn' disease	Nutritional deficits

Symptoms for Celiac disease and Risk Factors: Some of the most common signs and symptoms of celiac disease include.

Anemia, Anxiety, Bloating or gas, Brain fog, Constipation, Delayed growth in children, Depression, Diarrhea, Discolored teeth, Fatigue/tiredness, Headaches or migraines, Infertility, Irritability, Itchy skin rash (dermatitis herpetiformis), Joint pain, Pale mouth sores, Poor weight gain, Thin bones, Tingling/numbness [14, 16, 17]. Risk factors are: Down syndrome, Autoimmune Thyroiditis, Addison Disease, Microscopic Colitis and Type 1 Diabetes [15].

Treatment [18, 19]: It is carried out according to the following principles:

1. Giving balanced nutrition that includes all nutrients.
2. A completely glutinous diet.

3. You can eat alternative starches such as corn, soybeans and rice.

4. It is possible to start expressing milk in the first weeks of treatment, because the intestinal mucosa may not tolerate it temporarily, and then it is introduced gradually.

5. Replacing missing elements (iron, folic acid, Ca+2, Mg+2) [18, 19].

Epidemiology:

Seroprevalence Rate: 1.4% worldwide (1.3% in South America; 1.8% in Asia) (Am J Gastroenterol 2021; 116: 1148) [25]. Prevalence of biopsy diagnosed Celiac disease: 0.7% worldwide (Gastroenterology 2021; 160: 63) [26]. Mean age at diagnosis is 4-8 years. Bimodal distribution: first at 8 - 12 months and second in third to fourth decades [26, 27].

Associated with autoimmune diseases (dermatitis herpetiformis, type 1 diabetes mellitus, Hashimoto thyroiditis, Graves disease, *etc*.), idiopathic diseases (dilated cardiomyopathy, epilepsy, multiple sclerosis, *etc*.) and chromosomal diseases (Down syndrome, Turner syndrome and William syndrome) (BMC Med 2019;17:142 [28].

Patients with Celiac disease are at increased risk of cancer, including a twofold to fourfold increased risk of non-Hodgkin's lymphoma [27].

MATERIALS AND METHODS: Study was limited to a survey of the prevalence of Celiac disease in adult from non-immunological causes in two Syrian governorates (Homs and Tartous) with a population of about 5 million people, with ages exceeding 20 years. Statistics were collected from hospitals and clinics of gastroenterologists and nutritionists, during the period of 2014-2022.

This work was conducted at Al Hawash Private University Hospital (Dr. FarzatAyoub Hospital) as a research part of the College of Pharmacy project.

Data were collected from gastrointestinal clinics and hospitals in the two governorates in which the study was connected. Follow-up of Celiac disease cases and their development, as well as follow-up of intestinal biopsies and antibodies upon diagnosis, and after a gluten-free diet over a period of two years, was done by reviewing the relevant gastrointestinal clinics.

Test Manifestations: A simple blood test is available to test for Celiac disease. People with Celiac disease who eat gluten have higher than normal levels of certain antibodies in their blood, These antibodies are produced by the immune system because it views gluten as a threat. You must be on a gluten-containing diet for antibody (blood) testing to be accurate [6]. Typically, Celiac disease testing starts with antibody serology tests. If positive, they are often followed up with an upper endoscopy to confirm the diagnosis [16].

Xylose Tolerance Test: Xylose" also known as D-xylose" is a type of sugar that is easily absorbed by the intestines. The xylose test checks the level of xylose in both blood and urine [17]. Lower than normal levels can mean there is a problem with your body's ability to absorb nutrients.

Other Names: Xylose tolerance test, xylose absorption test, D-xylose tolerance test, D-xylose absorption test. Low results may also be due to an infection from a parasite, such as: proboscis worm Giardiasis. If blood xylose levels are normal, but urine levels are low, it may be a sign of kidney disease and/or malabsorption.

Lactose Tolerance Test: Lactose tolerance test: Lactose tolerance tests measure the body's ability to break down lactose [18, 19]. The lactase enzyme breaks down lactose into simpler sugars, which are absorbed by the body and converted into energy.

There are two types of Lactose Tolerance Tests:

Hydrogen Breath Test: This test measures the amount of hydrogen gas in the breaths before and after drinking a liquid containing lactose. It is the most common way to test for lactose intolerance.

Glucose Blood Test: This test includes a series of blood tests that measure the level of glucose in the blood before and after drinking a liquid containing lactose.

What do the results mean?

If you have a hydrogen breath test, the patient's results may show:

1. Increased hydrogen level after drinking lactose, this may mean that the patient has lactose intolerance.

2. A slight or no increase in hydrogen after drinking lactose, means that the patient's symptoms are probably not caused by lactose intolerance. (You may need further tests to find out the cause of your symptoms [18, 19].)

Intestinal Biopsy: Intestinal (duodenal) biopsy is considered the gold standard for diagnosis because it will inform doctors [20].

- If the patient suffers from celiac disease.
- If the patient's symptoms improve on a gluten-free diet due to the placebo effect.
- If the patient has another gastrointestinal disorder or allergy that responds to a change in his diet.
- If the results of antibodies or genetic screening tests are positive, the doctor may suggest an endoscopy.

Samples of the lining of the small intestine will be studied under a microscope to look for damage and inflammation caused by Celiac disease. It is recommended that the doctor take at least 4-6 duodenal samples from the second part of the duodenum and the duodenal lumen in order to obtain a diagnosis [20].

Sometimes the patient has an IgA deficiency and suffers from Positive in medical autopsy [21, 22].

RESULTS: 4,000 cases were recorded out of a current population of 5 million people, this means 0.08% of the population of these two governorates is infected with Celiac disease.

The patients' ages ranged between 20-33 years. In the **Table 2** we divided the recorded cases according to gender.

TABLE 2: SHOWS THE DISTRIBUTION OF PATIENT SAMPLES ACCORDING TO GENDER

Groups		Results
Gender	M	1480 (37%)
	F	2520 (63%)

The presence of HLA class II antigens was observed in all people with Celiac disease as HLA DQ2 was found in 82% of Celiac disease patients, and HLA DQ8 was found in the rest **Table 3.**

TABLE 3: SHOWS THE DISTRIBUTION OF PATIENT SAMPLES ACCORDING TEST RESULTS. IT SHOWED STATISTICAL DIFFERENCES

Tests	Result (% of patients)
HLA DQ2	3280 cases (82%)
HLA DQ8	720 cases (18%)

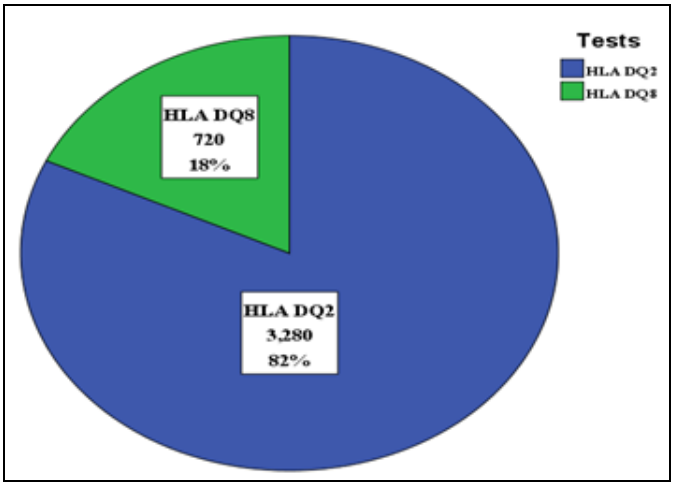

FIG. 2: THE DISTRIBUTION OF PATIENT SAMPLES ACCORDING TO TEST RESULTS

It is very important that follow-up showed that the results of antibody tests (Transglutaminase IgA) in patients adhering to the gluten-free diet decreased from 200 to 100 during a year of treatment, and to 20 during two years of treatment in all patients.

The decrease in antibodies was accompanied by a clear improvement in the absorption of iron and other elements, and a good improvement in the growth of intestinal villi in patients who underwent intestinal biopsies.

DISCUSSION AND CONCLUSION: The prevalence of Celiac disease has risen in recent decades and is currently about 1% in most Western populations. The reason for this rise is unknown [27].

Clinical features of Celiac disease include gastrointestinal and extra-intestinal symptoms because it is a systemic autoimmune disease that is triggered by dietary gluten [24, 31].

Among people who depend mainly on bread (wheat) rich in gluten, it is not possible to explain the rise of prevalence rate in adult, although it may relate to aspects of the hygiene hypothesis (exposure to micro-organisms and antibiotics). The

difference in the prevalence of Celiac disease between the sexes has not been explained by clear reasons, the results may be due to the male/ female ratio in the region. In the absence of Celiac disease many people identifying themselves as being gluten sensitive. The biological basis of gluten induced symptoms in the absence of Celiac disease is largely unknown but may be related to immune responses to components of wheat apart from gluten. It worth noticing that patients who adhered to gluten-free dietary protection and treated diseases concurrent with Celiac disease found a good result, meaning that the growth of intestinal epithelial cells, intestinal forests was gradually restored over a period of no less than three - five years of treatment. The current diagnosis of malabsorption disease is based on the demonstration of enteropathy in small intestinal biopsies and the presence of specific antibodies.

Diagnosing Celiac disease remains unknown. However, genetic background is an obligatory determinant of the development of Celiac disease and malabsorption along with environmental factors. New insights into malabsorption disease provide opportunities to intervene in its development, course, diagnosis, and treatment. However, lack of awareness of the gluten content of foods and the widespread incorporation of gluten into processed foods makes adherence to a gluten-free diet difficult. An important idea should not be forgotten that a portion of Celiac disease patients have a deficiency in total IgA, the prevalence of which among Celiac disease patients ranges from about 10 to 20 times its prevalence among the general population (1.7-3%) which should be taken into consideration.

The prevalence of Celiac disease among healthy adults is 1% in most regions of the world. Celiac disease has the characteristics of an iceberg epidemiologically, as there are many more undiagnosed cases than diagnosed cases. For every clinically diagnosed case of Celiac disease, there are several undiagnosed cases, either because they are hidden or silent, or because they are an asymptomatic condition.

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CONFLICTS OF INTEREST: Nil

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