Newsletter

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Al Borg Medical Laboratories 4th Newsletter

CELIAC DISEASE

UNDER-DIAGNOSED AND UNDER-TREATED

Celiac disease (CD) is an autoimmune disease that is characterized by a genetically-mediated, non-allergic, immunological response to the ingestion of gluten.

Celiac disease has emerged as an increasingly recognized Global health problem over the last half-century. Once considered a Western epidemic, It is now acknowledged as a common disease among Middle Eastern and North African populations.

Gluten is found in cereal grains such as wheat and barley. It is a protein mixture, composed largely of glutenin and gliadin.
Symptoms of CD are triggered when the grains are consumed. Currently, the only treatment is to maintain a strict gluten-free diet.
Undiagnosed and untreated, celiac disease can lead to the development of other autoimmune disorders, as well as osteoporosis, infertility, neurological conditions and in rare cases, cancer.

Populations at risk for CD

Prevalence is much higher in:

- First-degree (ten folds) and second -degree relatives of patients with CD
- Diabetes Mellitus (type 1)
- Down syndrome
- Turner syndrome
- Williams syndrome
- Selective IgA deficiency and other autoimmune disorders.

It is not uncommon for patients to be misdiagnosed or to experience a delay in the diagnosis of CD. It is estimated that only 3-15% of those with CD are diagnosed.

It is important for clinicians to be aware of high-risk groups susceptible to developing CD as these should be screened for the disease using serological tests.

Pathogenesis

Patients genetically susceptible to CD have human leukocyte antigens (HLAs) that recognize and bind gliadins. Bound gliadin stimulates the production of anti-gliadin antibodies. Certain gliadin polypeptides are resistant to gastric, pancreatic and intestinal peptidases and remain intact in the intestinal lumen. In individuals who are genetically-susceptible to CD, increased intestinal permeability allows additional gliadin polypeptides to enter the intestinal submucosa. Gliadin polypeptides deamidated by the intestinal enzyme tissue transglutaminases (tTG) initiate an immune response that creates anti-tissue transglutaminase autoantibodies (anti-tTG). These antibodies cause inflammation and damage the intestinal lining, restricting absorption of vital nutrients.

Anti-tTG antibodies also deposit in skin and brain as well as other tissues that contain tTG. CD patients can therefore have a spectrum of medical conditions other than malabsorption.

There are many factors which may trigger the onset of CD. In children, recurring gastrointestinal infections may play a role in the development of CD. In genetically susceptible adults who consume gluten, additional factors such as stress, surgery, pregnancy, or infections can result in acute CD symptoms.

Classification of CD

Recognition of the different clinical presentations of CD is important in order to accurately diagnose and decrease the risk of long-term complications.

Classical CD is dominated by symptoms of gastrointestinal malabsorption.

Atypical CD is characterized by non-prominent gastrointestinal manifestations with little or no symptoms. This may be the most common form of CD. Patients may present with chronic fatigue, anemia, dental enamel hypoplasia, reflux, bloating, migraines, osteoporosis, short stature, constipation, infertility, muscle weakness and/or depression.

Silent CD is described as asymptomatic patients with positive serological tests and villous atrophy on biopsy. This form of CD is usually diagnosed by screening high-risk individuals.

Latent CD is defined by positive serological tests, but with a normal small bowel biopsy. Patients are asymptomatic, but often develop symptoms and/or histological changes at a later date.

Diagnosis of CD

Who to test?

Serological testing is recommended for patients with:

- GI symptoms including chronic diarrhea, malabsorption, weight loss, and abdominal distension
- Unexplained persistent elevations of transaminases, short stature, delayed puberty, iron-deficiency anemia, recurrent miscarriages and infertility
- Irritable bowel syndrome
- Persistent aphthous stomatitis
- Other autoimmune diseases

- Peripheral neuropathy
- Cerebellar ataxia
- Dental enamel hypoplasia
- Those at higher risk of CD, *e.g.*, patients with type 1 diabetes mellitus, Down syndrome, Turner syndrome, Williams syndrome, or first or second degree relative with a confirmed diagnosis of CD.

Initial testing

Serological tests are the first steps to diagnosing CD in symptomatic patients. Confirmatory biopsy should be performed in positive cases. It is recommended to use multiple serological markers to achieve better clinical sensitivity and specificity.

Available tests include:

Serological tests

- Tissue Transglutaminase (tTG) IgA/IgG or endomysial antibody (EMA) has the highest sensitivity which varies between 84 and 88% and specificity greater than 90%. tTG is considered to be the most useful screening tool in adults
- IgG and IgA gliadins have poorer positive and negative predictive values for CD, but may be useful in screening children under the age of 18 months.
- 3-5% of celiacs are IgA deficient and 10 % of IgA deficient patients have CD. That's why Immunoglobulin IgA test should be started with to determine whether to use IgA or IgG tTG.

Intestinal biopsy

- To confirm a diagnosis of celiac disease, a biopsy of the small intestine is examined to detect damage to the intestinal villi. However, given the invasive nature and cost of a biopsy, antibody tests are often used to identify those individuals with high probability of having celiac disease.

Genetic testing

- 20-30% of the general population can have the genes, but only 0.1-1% may actually develop the disease.
- Due to their low positive predictive value, HLA-DQ2 and HLA-DQ8 testing is recommended mostly for exclusion when diagnostic and biopsy results are equivocal

Post diagnosis and monitoring

- Patients should have dietary instruction to recover from symptoms and avoid complications. Symptoms should disappear within 6-12 months of a strict gluten-free diet and blood tests should become negative.
- tTG IgA and IgG assays(based on IgA levels) every 3-6 months. Decline in antibody levels may correlate with normalization of the intestinal villi

- Patients should be assessed for deficiencies in vitamins and minerals, including fat-soluble vitamins, iron and calcium.
- Patients should undergo screening for osteoporosis.
- Children should have on-going evaluations to monitor growth and development.

Recommendations for Celiac Disease (CD) Testing in Children and Adolescents (ESPGHAN 2012)

European Society for Pediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) recommends testing for CD in children and adolescents

- **With unexplained**
  - Gastroenterological symptoms
  - Poor growth
  - Delayed puberty
  - Iron deficiency anemia
  - Abnormal liver testing
- **In the presence of the following risks for CD (even if asymptomatic)**
  - Autoimmune disorders – DM type 1, autoimmune thyroiditis, autoimmune liver disease
  - Genetic syndromes –Down syndrome, Turner syndrome, Williams syndrome
  - First degree relatives with CD
  - Selective IgA deficiency