guidelines

ADULT COELIAC DISEASE

The European Society for Primary Care Gastroenterology

Developed through an unrestricted educational grant from ThermoFisher Scientific
ESPCG guidelines on the diagnosis and management in primary care of adult coeliac disease

Definition

Coeliac disease (CD) is a chronic small intestinal immune-mediated enteropathy precipitated by exposure to dietary gluten in genetically predisposed individuals \(^{11}\). The diagnosis in adults is based on histological changes in biopsies taken from the duodenum of patients on a gluten-containing diet \(^{12}\).

Epidemiology

Several studies conclude that the overall prevalence of CD in Europe is about 1%, with a substantial proportion of the patients being undiagnosed \(^{12-14}\). There are significant differences between countries around Europe. A large-scale screening study of populations in Finland, Germany, Italy, and the UK found the prevalence to be highest in Finland (2.4%) and lowest in Germany (0.3%) \(^{12}\).

There is some evidence of an increase in the prevalence of CD over time, beyond what can be explained by the current focus on CD \(^{15}\).

The prevalence of CD in other regions of the world is also relevant to general practitioners (GPs).

The estimated prevalence of CD in the US is 0.7% in the total population, but 1.0% among non-Hispanic whites \(^{16}\). The prevalence is also comparable to Europe in other regions with a high proportion of inhabitants of European origin, like Australia, New Zealand, and South America, and CD is also prevalent in North Africa and the Middle East. In Sub-Saharan Africa and in the Far East CD is rare, but good data are lacking. In these areas the gluten content in the diet is much, and there is also a lower frequency of the predisposing HLA-related genes \(^{16}\), although not negligible \(^{16}\). The risk of CD might increase if genetically predisposed people migrate and introduce more gluten in their diet.

Some studies have found a higher prevalence among females \(^{8,14}\), but this was not found in screening studies \(^{16}\), and the observed gender difference in diagnosed patients might be a result of different health care seeking behaviour.

There is an important genetic component in CD, and the prevalence among first-degree relatives of patients diagnosed with CD is 10% \(^{14}\). Studies also show that more than 99% of CD patients are positive for either HLA-DQ2 or HLA-DQ8 \(^{12,13}\).
Clinical symptoms

Classical CD shows manifestations of malabsorption with symptoms like diarrhoea, steatorrhea, weight loss, and growth failure in children. Some patients will present with iron deficiency anaemia, folate deficiency or vitamin B12 deficiency (1). When CD presents without malabsorption it is termed “non-classical”, and this, together with asymptomatic CD, is now more common in newly diagnosed patients than previously (14). Patients may present with a wide range of symptoms and signs: anaemia, unspecific or vague abdominal symptoms, neuropathy, ataxia, depression, short stature, osteoporosis, elevated liver enzymes, infertility, adverse pregnancy outcomes and lymphoma.

In patients with chronic symptoms the severity may be difficult to assess, and the presence of symptoms may not be recognized by all patients with CD. In some cases the presence of symptoms is not acknowledged until some time on a gluten-free diet (15, 16).

Related conditions

CD is associated with several other conditions and this should be taken into consideration both in diagnostic interventions and in the follow-up of diagnosed patients.

The prevalence of CD is increased in patients with irritable bowel syndrome (4%) (17), diabetes mellitus type I (3-6%) (18), osteoporosis (1-3%) (18, 19), Down’s syndrome (10%) (20), and thyroid disease (21).

Dermatitis herpetiformis (DH) is a skin condition triggered by dietary gluten and the diagnosis is made by detection of perilesional granular IgA deposits. DH can be present without CD, 25% of the patients in one study had no villous atrophy (22). The prevalence is much lower than for CD with large regional variations. It is rare outside Northern Europe and areas with people of North European origin (23), and the highest reported prevalence was 0.08% in a study from Finland (24).

Who should be tested for CD?

Symptomatic patients
- Patients presenting with symptoms of malabsorption
- Low threshold for testing in patients with nonspecific symptoms associated with CD.

Patients at increased risk
- Asymptomatic first degree relatives of patients with confirmed CD should have the opportunity to discuss testing with their GP
- Patients with irritable bowel syndrome, diabetes mellitus type I, Down’s syndrome and dermatitis herpetiformis should be offered testing for CD
- Consider testing in patients with CD associated conditions; premature osteoporosis, thyroid disease, unexplained elevation of liver enzymes, dental conditions (enamel loss), infertility

Screening
- The criteria for population screening are not met for CD and systematic or opportunistic screening should not be performed (25)
Follow up in primary care

CD is associated with several other conditions and this should be taken into account. The treatment for CD is lifelong and requires strict adherence to a gluten-free diet. However, non-adherence is reported by up to 70% of patients and may be intentional or inadvertent. Intentional non-adherence is associated with low self-efficacy and perceived tolerance to gluten. There will be different resources available for support and follow-up throughout Europe, but possible services include dieticians, practice nurses, gastroenterologist, general practitioners, and other health care professionals with an interest in CD. Patients have expressed a preference for seeing dieticians for long term follow-up. Patient organizations will often have extensive programs for information, counselling and guidance on how to maintain a gluten-free and yet palatable diet.

There is no consensus on recommended frequency or content of follow-up. Most recommend annual assessment, and depending on the health care system different professionals could be involved. Since CD is a lifelong chronic condition GPs can play an important role in the follow-up of this group of patients.

Points for follow up should be guided by the clinical condition and the views of the patient and should include:

- Assessment of adherence to a gluten free diet and symptom control
- Assessment of possible associated co-morbidities
- Laboratory testing (indicators of malabsorption (Hb, markers of iron deficiency, folate, vitamin B12, calcium, albumin), indicators of adherence to diet (serological markers))
- Assessment of the risk of osteoporosis and the need for bone density measurement

Persistent gastrointestinal symptoms in spite of strict adherence to a gluten free diet could be a result of coexisting conditions like IBS, lactose intolerance, bacterial overgrowth or inflammatory bowel disease. Further investigations, including referral to a gastroenterologist, should be considered.

New symptoms in a patient on a gluten free diet should not be automatically attributed to CD, but be investigated independently.

How to investigate?

First line investigation in patients on a gluten containing diet is serological testing for IgA anti-tissue transglutaminase antibodies (IgA-TG2, also a-TTG, TTA, or TTGA). The test has a sensitivity of 89% and specificity of 98% in the primary care setting. Deamidated antigliadin antibodies (IgA-DGP or IgG-DGP) show similar performance and are an alternative or supplement to IgA-TG2. Antibodies against native gliadin (AGA) were previously key in the investigation of CD, but they have significantly lower sensitivity and specificity and should no longer be used in routine testing.

In patients already on a gluten free diet HLA genotyping (HLA-DQ2/DQ8) can be used to rule out CD or the risk of later developing CD. If HLA-DQ2 or HLA-DQ8 is present serological testing can be done after gluten challenge lasting at least 14 days (i.e 2 slices of wheat bread daily (≥3g gluten)). If still negative the period of gluten challenge can be extended to six weeks.

The prevalence of IgA deficiency is 2-3% in patients with CD, significantly higher than in the general population. Measuring total IgA should be considered initially in patients with high pretest probability of CD, or later in patients with negative IgA-TG2. Patients with IgA deficiency should be tested for IgG-TG2.

Patients with a positive serological test should be referred to a gastroenterologist for gastroscopy and biopsy while still on a gluten-containing diet in order to confirm the diagnosis.

Patients with negative serological test, but with classical symptoms of CD (signs of malabsorption) and/or symptoms or signs of other upper gastrointestinal diseases should be referred to a gastroenterologist for gastroscopy and assessment.

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References:

By Primary Care For Primary Care

**Advisory Board for Adult Coeliac Guidelines**

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Knut-Arne Wensaas is a general practitioner and specialist in family medicine working in Bergen on the western coast of Norway. He is a senior researcher at the Research Unit for General Practice, Uni Research Health, and an associate professor at the Department of Global Public Health and Primary Care, University of Bergen. He defended his Ph.D.-thesis in November 2012: “Irritable bowel syndrome and chronic fatigue following infection with Giardia lamblia. Preliminary factors and long-term consequences.” Professor Wensaas is a former president of the ESPCG, and is the leader of the Network Group for Gastroenterology of the Norwegian College of General Practice, the national group of ESPCG.

**Professor Juan Mendive, Spain (Chair of the ESPCG)**
Juan Mendive trained at the University of Navarra and in Barcelona, where he completed his PhD. Now a trainer in family medicine, and a member of the Spanish Primary Care Research Network (RedAIF) as well as an active family physician, Dr. Mendive's interests include gastroenterology and mental health education in primary care. His involvement in international groups ranges from WONCA, where he has been the Spanish representative, to the ESPCG, where he is a founder member of the steering group.

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**Dr. Pierluigi Fracasso, Italy**
Dr. Pierluigi Fracasso, born in Rome in 1960, works as a Gastroenterologist in an Outpatients clinic in Rome, Italy. He focused his interest on the prevention of gastrointestinal cancers, studying high-risk conditions (IBD, HP, FAP, Coeliac disease) and screening average-risk populations and compliance with testing. He is Secretary of the European Society of Primary Care Gastroenterology and an affiliate of the Italian Association of Primary Care Gastroenterology.

**Professor Richard Stevens, United Kingdom**
Richard Stevens is the Editor in Chief of The Digest and EuroDigest. A founder member of the UK Primary Care Society for Gastroenterology, he is also the Society’s chairman. Dr. Stevens studied Psychology and Physiology at Oxford before his medical degree. A GP principal, trainer and tutor in Oxford for nearly three decades, he was also a practitioner in endoscopy at the John Radcliffe Hospital. He has been involved in a number of research projects and writes on gastrointestinal and other topics for a range of publications.

**Professor Lars Agréus, Sweden**
Lars Agréus has been Professor of Family Medicine at the Karolinska Institute in Sweden since 2007 and was head of the department of Family Medicine at Karolinska Institute between 2009 and 2013. In addition to his former role as President of the ESPCG, he has chaired the European Society for Family Medicine since 2012, is also chair of the Swedish Society for Rural Medicine and, since 1981, has worked as a rural general practitioner in Örnsund Osthammar, where his ‘standard rural medicine duties’ include emergency medicine. Professor Agréus presented his thesis ‘The Abdominal Symptom Study’ in 1993 and completed his post-doctoral year with Professor Nicholas J Talley at the University of Sydney. His subsequent research has focused on population-based endoscopy studies. He runs an international research group with world authorities in gastroenterology, microbiology, histology and genetics, and has published around 60 scientific articles in leading peer-reviewed journals. Professor Agréus received the Rome Foundation research award in 2011.

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Pali Hungin is Professor of Primary Care and General Practice and was previously the Dean of Medicine, Durham University, UK. In addition to medical education, his main interest is in the earlier diagnosis of clinical problems and evidence-based implementation of care, especially in difficult-to-reach settings such as care homes. He has published extensively on reflux disease and functional GI disorders. Professor Hungin is a founding member of the UK and European Primary Care Societies for Gastroenterology and Chair of the Rome Foundation Primary Care Committee. He also served on the Scientific Committee of the United European Gastroenterology Federation and the Guidelines Committee of the World Gastroenterology Organisation.

**Professor Jean Muris, The Netherlands**
Jean Muris is Professor in Family Medicine and Director of the residency training family medicine at the Maastricht University, Maastricht, the Netherlands. He coordinates also a research group in the research school CAPPHI and is involved in studies on colorectal cancer screening, and IBS (www.capphi.nl).

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