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SHORT REVIEW

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# A new insight into non-specific abdominal pain

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ABSTRACT

This review aims to change clinical practice and alert clinicians to consider that unrecognised coeliac disease may present acutely with abdominal pain. Targeting patients who have non-specific abdominal pain or coeliac-associated symptoms/diseases may improve diagnosis.

KEYWORDS

Non-specific abdominal pain – Coeliac disease

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Acute abdominal pain accounts for up to 50% of emergency surgical admissions.[1] Computer-aided diagnostic questionnaires, abdominal ultrasound, computed tomography (CT) scan of the abdomen, early laparoscopy and peritoneal aspiration (with neutrophil counting) have all been described as potential methods for improving the diagnostic yield in this group of patients.[2] However, despite these advances, a cause for the patient's symptoms may not always be recognised. As a result, surgeons have internationally described the entity of non-specific abdominal pain (NSAP).[3] This is defined as 'pain for which no immediate cause can be found (during the acute admission) and specifically does not require surgical intervention'. NSAP may be self-limiting and accounts for 13–40% of all surgical admissions.[4] Follow-up of this cohort of patients has revealed diverse clinical outcomes. De Dombal (who originally classified this entity) reported that up to 10% of patients with NSAP were subsequently found to have an intra-abdominal malignancy (if over the age of 50 years).[5] Gynaecological causes of NSAP have also been recognised. Conversely, other investigators have suggested a more favourable outcome, with 77% of patients with NSAP being symptom-free at 5-year follow-up. More recently, an association between NSAP and irritable bowel syndrome (IBS) has been described suggesting that there may be a functional aspect to NSAP.[6]

## The relationship between non-specific abdominal pain and coeliac disease

Abdominal pain may be a presenting feature of coeliac disease. The prevalence of adult coeliac disease in the general population has been reported to be in the magnitude of one per 100–200. This has been determined by epidemiological studies screening cohorts of healthy volunteers in the US, UK and other European countries.[7] Coeliac disease or gluten-sensitive enteropathy is defined as a state of heightened immunological responsiveness to ingested gluten (from wheat, barley or rye) in genetically susceptible individuals. Patients with coeliac disease may initially be recognised by using non-invasive serological tests. The positive predictive value of these serological markers (IgG/IgA antigliadin antibodies, tissue transglutaminase and endomysial antibody) is in excess of 90%. In the presence of a positive antibody, the diagnosis of coeliac disease should be confirmed by performing a duodenal biopsy. Histological demonstration of small bowel villous atrophy remains the 'gold standard' for making the diagnosis of coeliac disease.

Patients with adult coeliac disease typically complain of gastrointestinal symptoms suggestive of malabsorption. This manner of presentation is now described as the classical (typical) form. The increasing recognition of this condition is attributed to novel serological assays and the realisation that patients do not always have gastrointestinal symptoms (silent or atypical form) but may present insidiously, for example with iron-deficiency anaemia, osteoporosis, cryptogenic hypertransaminasaemia, or neurological symptoms.

We have previously described an association between coeliac disease and IBS.[8] In addition, we demonstrated that patients' symptoms improved on a gluten-free diet. When we retrospectively assessed how patients with coeliac disease presented in our centre, 16.3% had abdominal pain and many had previously been seen in surgical departments or had a gastroscopy without duodenal biopsy prior to their diagnosis. The mean delay in diagnosis in our cohort was 5 years (range, 0.25–16 years) and this is consistent with the literature. Other investigators have reported that patients with undiagnosed coeliac disease are more likely to have surgical interventions (appendicectomy and cholecystectomy) when

compared to age- and sex-matched controls.[9] Despite coeliac disease affecting up to 1% of the population, meta-analysis has suggested that the ratio of known to undiagnosed coeliac disease is about 1 to 7. This suggests a failure in case-finding for coeliac disease.

Based on these previous observations, we hypothesised that patients presenting with acute/surgical abdominal pain could have unrecognised coeliac disease. There have been no previous controlled studies evaluating this approach.[10] A case-control study was undertaken involving 300 consecutive new unselected patients presenting with acute abdominal pain (in a university hospital in the UK), and healthy controls (age- and sex-matched) without abdominal pain ($n$ = 300). We initially used a panel of coeliac antibodies (as previously described). Any patient with a positive antibody result had a duodenal biopsy to confirm the diagnosis. Coeliac disease was diagnosed in 3% of patients who presented with unselected acute abdominal pain to secondary care. Compared with matched controls, the association of acute abdominal pain with coeliac disease gave an odds ratio of 4.6. ($P$ =0.068; 95% CI, 1.11–19.05). When only considering NSAP (which accounted for 28.6% of our cohort; 86/300) the prevalence of coeliac disease was highly significant at 10.5% (9/86; $P$ = 0.006). Patients' symptoms improved on a gluten-free diet at 12–18-month follow-up. Although our observations are unique for an adult population, these findings are potentially validated by the subsequent improvement of these individuals' symptoms on a gluten-free diet. In addition, there have been similar reports of coeliac disease presenting with recurrent abdominal pain in the paediatric population.[11,12]

## The cause of abdominal pain in patients with coeliac disease

The mechanism of abdominal pain in coeliac disease is not clear. Historically, reports have described coeliac disease presenting with pseudo-obstruction[13] (secondary to hypokalaemia) or with small bowel obstruction secondary to lymphoma.[14] An association between coeliac disease and idiopathic recurrent pancreatitis has also been suggested.[15] However, none of the patients in our study with coeliac disease had any indication of these clinical features and all had a normal serum amylase. Small bowel intussusception was previously considered to be a feature of asymptomatic coeliac disease;[15] more recently, a few symptomatic cases have been reported.[17,18] Alternative hypotheses could be related to reversible autonomic dysfunction of the gastrointestinal tract or IBS.[7,19]

## Modification of clinical practice

The investigational pathway for patients with acute abdominal pain is well established. Following clinical assessment, if the surgical team deems that further investigations are necessary, then a full blood count, urea, electrolytes, amylase, C-reactive protein (CRP) and random glucose are undertaken as baseline tests. Urine analysis, erect chest and abdominal X-rays may be requested selectively.[2,3,20,21] Further investigations including contrast enema, abdominal/pelvic ultrasonography or abdominal CT may also be performed; however, imaging is generally only arranged following senior review.[2,21] We suggest that, at any point throughout this assessment, if a patient is considered not to have acute abdominal pain warranting surgical intervention or their symptoms are described as NSAP, this should alert the clinician to consider the diagnosis of coeliac disease. The use of a coeliac antibody profile at this stage is a cheap and non-invasive test (in our centre about £25). The combination of EMA and TTG will provide a positive predictive value in excess of 90%.[8,10] Recognition or questioning for coeliac-associated symptoms/diseases (*e.g.* iron-deficiency anaemia) may further improve diagnostic yield. This approach may not only help in making the diagnosis but also has the potential to avoid further investigation.

## Conclusions

Clinicians should consider that unrecognised coeliac disease may present acutely with abdominal pain. Targeting for this diagnosis to patients who have NSAP or coeliac-associated symptoms/diseases may improve the diagnostic yield.

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# Dual publication and the watchful referee

Journal editors deplore dual publication, which overloads the literature with redundant references, and which can inappropriately inflate an author's publication list. The Editors of the Annals are no exception, and their unwillingness to accept or condone attempted or actual dual publication extends to review articles as well as original papers.

Recently the Editors have had cause to be grateful to a sharp-eyed referee, who pointed out that a review submitted to the Annals was substantially the same as a previous review article by the same two authors, published in an American journal. That earlier publication had been accepted in early 2004, and appeared later that year. The review submitted to the Annals contained a handful of extra references, but most of the text was very similar and, in places, whole sections were identical to the earlier publication. Most tellingly, the authors chose not to refer to this earlier publication in the present submission.

The Committee on Publication Ethics (<www.publicationethics.org.uk>) has developed guidelines on good publication practice. They define redundant publication as 'when two or more papers, without full cross reference, share the same hypothesis, data, discussion points or conclusions'. The Committee recommends 'at the time of submission authors should disclose details of related papers even if in a different language, and similar papers in press'.

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In this case, the review article was not accepted for publication.

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