

## ORIGINAL ARTICLE

# Changing face of adult coeliac disease: experience of a single university hospital in South Yorkshire

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*Postgrad Med J* 2002;78:31–33

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Submitted 20 April 2001  
Accepted 3 July 2001

**Objective:** To determine the incidence and presenting features of adult coeliac disease in a single university hospital in South Yorkshire.

**Design:** A retrospective case finding study. Data were obtained from pathology and immunology databases, clinical notes, dietetic records, and patient questionnaires.

**Setting:** Royal Hallamshire Hospital in South Yorkshire, England.

**Participants:** All recorded cases of coeliac disease.

**Main outcome measures:** Crude annual incidence rates for coeliac disease was obtained. The numbers of coeliac antibody profiles requested per year from the Royal Hallamshire Hospital were ascertained. Age at diagnosis, sex, year of diagnosis, presenting symptoms, associated conditions, and delay in diagnosis was documented. In addition the speciality of the clinician who made the diagnosis was noted.

**Results:** There were 264 cases in total (male n=86, ratio 1:2). Mean age at diagnosis was 44.9 years (range 1–82, median 44.5). A trend was observed from 1990 to 2000 inclusive, of an annual increase in the incidence of coeliac disease. There has been a coincidental increase in the measurement of associated antibodies. Although 28.4% of patients presented with *gastrointestinal* symptoms, 20.1% had iron deficiency anaemia. The ratio of typical to atypical symptoms was 1:2.5. (single sample test of proportions  $p<0.001$ ). The diagnosis was made by a gastroenterologist in only 52.7% of cases. The median duration of symptoms before the diagnosis of coeliac disease was 4.9 years (range 0.25–16 years).

**Conclusion:** Coeliac disease is now presenting more commonly without gastrointestinal symptoms and often to specialties other than gastroenterology. Although more cases are diagnosed, this may be a reflection of increasing recognition rather than a true increase in incidence.

In the last decade there have been considerable advances in our understanding and recognition of coeliac disease.<sup>1</sup> The prevalence of adult coeliac disease in western European populations is considered to be in the magnitude of one per 200–300 *individuals*.<sup>1,2</sup> This has been determined by epidemiological studies screening cohorts of healthy volunteers.

We now recognise that patients with adult coeliac disease do not always complain of gastrointestinal symptoms suggestive of malabsorption, the so-called classical (typical) form.<sup>1,3,4</sup> Increasingly patients are being diagnosed who have no gastrointestinal symptoms (silent or atypical form) but may present insidiously for example with, iron deficiency anaemia,<sup>5</sup> osteoporosis,<sup>6</sup> ataxia, or peripheral neuropathy.<sup>7</sup>

Previous investigators have suggested that there may be a true increase in the incidence of coeliac disease, although this issue is controversial.<sup>8–10</sup> This observation could be related to our increasing recognition of different forms of coeliac disease or the development of novel antibody tests for coeliac disease which provide an effective non-invasive means of screening high risk patients.<sup>11</sup>

We therefore determined our experience of coeliac disease to ascertain whether there were increasing numbers of cases being diagnosed or if the symptoms of presentation were changing.

## METHODS

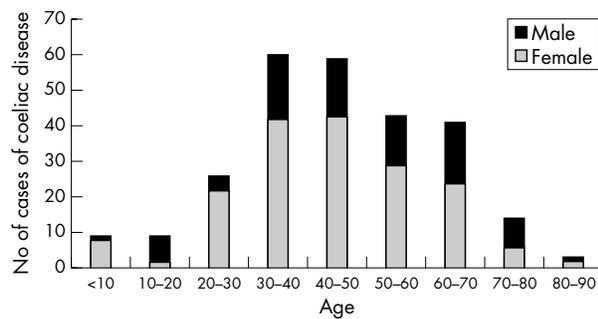
We undertook a retrospective case finding study at a single university hospital in South Yorkshire, England. The population served is approximately 250 000. The city of Sheffield is demographically representative of urban England and thought to have a stable population.<sup>12</sup>

Cases of coeliac disease were identified using dietetic records as well as pathology and immunology databases. All patients with coeliac disease were confirmed by endoscopic small bowel biopsy. The histological features consistent with coeliac disease included crypt hyperplasia, villous atrophy, an increase in intraepithelial lymphocytes to more than one lymphocyte per six epithelial cells and the absence of other significant pathology. This is in accordance with the revised ESPGAN criteria.<sup>13</sup>

Data collected included patient demographics, delay in diagnosis, symptoms at the time of presentation, and whether they had any coeliac related conditions. Patients with coeliac disease were sent a postal survey pertaining to any delay in diagnosis and their duration of symptoms before diagnosis. Confirmation of these details was obtained by retrospective case note review. If patients had presented to other specialties with coeliac associated symptoms before their diagnosis, this was recorded.

The speciality of the doctor who made the initial diagnosis was determined according to who had requested duodenal biopsy or the coeliac antibody profile. The immunology department provided information regarding cases with positive antibodies and annual rates of antibody profiles performed in our hospital. Pathology records have been stored on SNOMED since 1994 and before this categorisation is according to histological diagnosis.

Statistical analysis of data were performed using Stat-view 4.5 (Abacus Concepts). Comparisons between patients with typical and atypical symptoms were made using a single sample test of proportions.



**Figure 1** Age and sex of patients with coeliac disease at the time of their diagnosis.

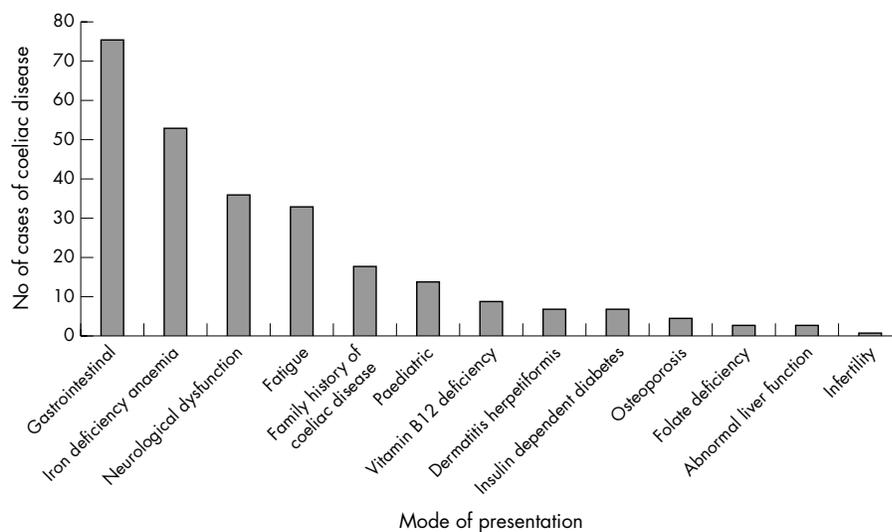
**Table 1** Gastrointestinal symptoms described at presentation by patients with "typical" coeliac disease (n=75)

Symptom	No with symptom (n=75)	Coeliac patients with typical symptoms (%)
Diarrhoea	52	69.3
Constipation	2	2.7
Steatorrhoea	3	4.0
Abdominal distension	25	33.3
Abdominal pain	43	57.3
Flatulence	21	28.0
Borborygmus	26	34.7
Tenesmus	39	52.0
Reflux	11	14.7
Nausea	3	4.0
Vomiting	4	5.3

## RESULTS

There were 264 cases in total. There were 86 males and 178 females (sex ratio 1:2). The mean age at diagnosis for the whole cohort was 44.9 years (fig 1). There were no significant differences between sexes: males (n=86), median 42.9 years, range 1–82 and females (n=178), median 45.2 years, range 1–81.

The most common manner of presentation was gastrointestinal, accounting for 28.4% of cases (fig 2). However when subanalysing this cohort of patients, although diarrhoea was the predominant complaint (69.3%), there were many patients who had other gastrointestinal symptoms which are not normally attributed to malabsorption (table 1). The paediatric



**Figure 2** Mode of presentation of patients with coeliac disease.

**Table 2** Number of cases diagnosed according to the speciality of the investigating clinician

Specialty	Coeliac disease cohort (%)	No of cases of coeliac disease
Gastroenterologist	52.7	139
Consultant physician with other speciality interests	28.4	75
Surgeon	6.8	18
General practitioner	6.8	18
Paediatrician	3.8	10
Obstetrician	1.1	3
Self diagnosed by patient	0.4	1

atric cases were those patients who had been transferred to adult care or represented having originally had the diagnosis made as a child but been lost to follow up. However confirmation of coeliac disease was still ensured by duodenal biopsy in our centre (fig 2).

Classifying patients presenting symptoms according to whether they were typical or atypical revealed no statistical differences on a year by year basis. Nevertheless, when considering the whole cohort this was significant, typical: atypical, 1:2.5 ( $p < 0.001$ ).

The diagnosis of coeliac disease was made by a gastroenterologist in only 52.7% of cases and many other specialties are now recognising this condition (table 2).

Before 1990 there were 48 cases of coeliac disease documented. Since 1990 there has been an increase in the number of new cases almost annually (table 3). Antibody profiles as a means of non-invasively screening patients with symptoms for coeliac disease was first introduced into our clinical practice in 1994. This was initially antigliadin antibody (IgG and IgM) and more recently in 1997 antiendomysial antibody. Since the introduction of antibody screening the number of tests performed has increased annually (table 2).

The median duration of symptoms before diagnosis of coeliac disease was 4.9 years (range 0.25–16 years). Seventy six patients (28.8%) had seen consultants in other specialties with coeliac associated symptoms. However their complaints were not attributed to coeliac disease until representing at a later date. Thirty six (13.6%) patients had previously been investigated by surgeons and underwent gastroscopy for investigation of gastrointestinal symptoms without having antibody testing or duodenal biopsies.

**Table 3** Number of cases of coeliac disease diagnosed by year with corresponding rates of antibody profiles performed

	Pre-1990	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000
New coeliac diagnoses	48	2	3	5	4	3	12	18	24	41	50	54
Antibody profiles	0	0	0	0	0	12	12	48	120	240	372	1464

## DISCUSSION

This study demonstrates that increasing numbers of patients are being diagnosed with coeliac disease. However this may not be a true increase in incidence as there is a coincidental rise in the number of antibody profiles performed. Hawkes *et al* made similar observations in Wales.<sup>10</sup> He postulated that a real increase in incidence should also be seen in patients with dermatitis herpetiformis as these two conditions share the same genetic inheritance. This has not been confirmed and would substantiate the view that the increasing incidence is a reflection of our evolving recognition of the heterogeneous nature in which coeliac disease may present. Our data also provide evidence to support this: atypical symptoms were 2.5 times more common than the classically described gastrointestinal presentation. In particular iron deficiency anaemia accounted for 20.1% of all cases. This changing pattern of symptoms in patients with coeliac disease has been described by other investigators.<sup>5,9</sup>

Coeliac disease is underdiagnosed and the case finding strategy employed by Hin *et al* would seem a valid approach.<sup>14</sup> In this study the selection criteria for screening patients in primary care was based on symptoms potentially attributable to coeliac disease or coeliac associated conditions. Hin screened a cohort of 1000 high risk patients and diagnosed 30 new cases of coeliac disease.<sup>14</sup>

A significant number of patients in our study had gastrointestinal symptoms but not those necessarily considered to suggest malabsorption. Given that 13.6% of our cohort underwent gastroscopy without duodenal biopsy some time before their diagnosis, a high level of clinical suspicion should be present when evaluating patients with any gastrointestinal symptoms. A recent study from Northern Ireland reported eight new cases of coeliac disease when 150 patients referred for routine upper gastrointestinal endoscopy had small bowel biopsies performed irrespective of whether their symptoms were suggestive of coeliac disease.<sup>15</sup> Only two of the individuals with coeliac disease had symptoms of malabsorption or anaemia.

Despite an almost annual increase in the number of new cases of coeliac disease there is still a delay in the recognition of this condition. Our median duration of symptoms before diagnosis was 4.9 years; this is comparable with previous reports.<sup>3, 10, 16</sup> Of interest is the observation that only 52.7% of cases were diagnosed by a gastroenterologist. This would suggest that other medical specialties are now more aware of the alternative manners of presentation of coeliac disease.

There are limitations to this study. The ability of patients to recall information regarding delays in diagnosis or previous consultations may not be accurate. However case note review provided an alternative means of substantiating these data. Given the retrospective nature of our study it is possible that some cases of coeliac disease that were diagnosed before 1990 have been lost to follow up. This discrepancy may be reduced by the use of several recorded sources to trace patients with coeliac disease. We had a disproportionate number of coeliac patients presenting with neurological dysfunction (n=36). This may reflect our own specialist interest.<sup>7</sup>

The benefits of early recognition of coeliac disease are well described. The coeliac disease related complications of osteoporosis,<sup>8</sup> anaemia,<sup>5</sup> an increased risk of malignancy,<sup>17</sup> and

infertility<sup>18</sup> are all potentially reversible on a gluten free diet. The increased awareness responsible for the increasing numbers of coeliac disease recognised needs to continue, perhaps together with a lower threshold for screening high risk patients using antibody profiles, which are cheap, non-invasive, and may prevent delays in diagnosis for the individual.

## ACKNOWLEDGMENT

We wish to acknowledge the support of Action Research. Dr Sanders is entirely funded by Action Research as an Action Research Training Fellow.

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