

# Coeliac disease: clinical presentations, correlations of dietary compliance, symptomatic response and repeat biopsy findings

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## SUMMARY

*Gastrointestinal symptoms were present at the time of diagnosis in 81 (76%) of 107 patients with coeliac disease: 56% had diarrhoea / steatorrhoea, 32·7% abdominal pain and 15% constipation. Gastrointestinal symptoms were commonest in young adults (20–39 years) and less frequent in children (0–19 years).*

*Anaemia, low serum levels of folic acid, albumin and calcium, and raised serum alkaline phosphatase may be of help in raising the index of diagnostic suspicion, but in over half of our patients with clinically and histologically active disease these values were within normal limits.*

*In patients adhering to a gluten free diet remission of symptoms correlated well with histological response; the continuation of symptoms indicated a higher incidence of histological abnormality. No patient not complying to the diet had normal histology on repeat biopsy. Five patients died over the ten year period, one from a small bowel lymphoma.*

## INTRODUCTION

Classical coeliac disease presenting with diarrhoea / steatorrhoea, abdominal pain, weight loss and abdominal distention presents a relatively easy diagnostic problem which is definitively solved on jejunal biopsy. Once started on a gluten free diet most patients improve clinically and the jejunal villous pattern should return to normal. Not all patients present in this classical fashion and symptomatic response does not necessarily correlate with return to a normal villous pattern.

We studied 107 patients and reviewed their clinical presentations in conjunction with the haematological and biochemical tests. We correlated disease activity on biopsy to symptoms, and to dietary compliance. We also studied prognosis

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particularly in comparison to a similar study carried out in the Royal Victoria Hospital, Belfast.

## MATERIALS AND METHODS

We reviewed the records of all patients with subtotal villous atrophy on jejunal biopsy in the gastroenterology department of Jervis St. Hospital, Dublin between October 1975 and April 1986. A diagnosis of coeliac disease was accepted if, in the appropriate clinical setting, the histology revealed subtotal villous atrophy.<sup>1</sup> The age at diagnosis, age at onset of symptoms, duration of follow up and relevant family history were identified. The reasons for performing the biopsy were identified and symptoms present at time of the biopsy diagnosis noted.

Patients were classified into those who claimed to be adhering to a gluten free diet and those who said they were not keeping to the diet: no dietetic assessment of these claims was made. Differences between groups were tested for significance using Chi squared analysis, with Yates correction.

## RESULTS

The diagnosis of coeliac disease was made in 107 patients, 73 female (68.2%) and 34 male (31.8%). A positive family history was noted in 19 patients, and 15 of the patients in this study were related to at least one other study member. Forty two were diagnosed below age 20 years, forty between 20 and 40, and only five over the age of 60, two of these being over 70 years. Twelve of the 107 patients had been lost to follow up. The average duration of follow up of the remaining 95 patients was 9.2 years.

Gastrointestinal symptoms were the commonest indication for biopsy (81 patients). Symptoms at presentation were diarrhoea/steatorrhoea (60 patients), abdominal pain (35), constipation (16), lethargy (16), and weight loss (9): fainting, paraesthesia, bone pain, anorexia and abdominal swelling occurred only in a few patients. Gastrointestinal complaints as an indication for biopsy between the different age groups are summarised in Table I.

TABLE I  
*Symptoms related to patient age*

	<i>Age group (years)</i>			
	<i>0-19</i>	<i>20-39</i>	<i>40-59</i>	<i>60+</i>
<i>Total</i>	42	40	20	5
Gastrointestinal symptoms	25 (60%)	38 (95%)*	14 (70%)	4 (80%)
Diarrhoea/steatorrhoea	24 (57%)	22 (55%)	11 (55%)	3 (60%)
Abdominal pain	14 (33%)	17 (42%)	4 (20%)	0
Constipation	5 (12%)	3 (8%)	4 (20%)	4 (80%)
Weight loss	5 (12%)	2 (5%)	2 (10%)	0
Anorexia	0	0	3 (15%)	0
Abdominal swelling	2 (5%)	0	0	0
Vomiting	0	0	0	0

\*Significantly greater than the 0-19 ( $p < 0.001$ ) and 40-59 ( $p < 0.01$ ) age groups.

Forty six (45%) of 21 patients were anaemic at presentation (Hb < 12.0 g/dl): 20 (21%) were macrocytic and 15 (14%) microcytic. Serum folic acid was less than 2.0 mg/dl in 42 (39%). Hypoalbuminaemia (< 40 g/l) was found in 45 (42%), hypocalcaemia (< 2.1 mmol/l) in 28 (26%) and an elevated serum alkaline phosphatase (> 250  $\mu$ /l) in 27 (25%).

Information concerning dietary compliance or lack of it and the results of further biopsies are shown in Table II.

TABLE II  
*Claimed adherence to gluten free diet in 95 patients*

	No	<i>Result of repeat biopsy</i>		
		<i>Normal</i>	<i>Abnormal<sup>+</sup></i>	<i>Not done</i>
<u>Complying with diet (75)</u>				
Remission of symptoms	48	31	9	8
Improvement in symptoms	24	5	9	10
No change	3	1	1	1
<u>Not complying with diet (20)</u>				
Remission of symptoms*	2	0	2	0
Improvement in symptoms	11	0	8	3
No change	7	0	4	3

+Abnormal; either subtotal or partial villous atrophy.<sup>1</sup>

\*The two patients who claimed remission of symptoms despite non adherence to a gluten free diet had both initially adhered to their diets and had normal jejunal biopsies, but reverted to subtotal villous atrophy on stopping their diet.

Five patients died over this ten year period, two from malignancy, and one each from pulmonary embolus, cerebrovascular accident and myocardial infarction. Of those dying from malignancy one had a small bowel lymphoma and the other a cerebral glioma. The patient with lymphoma had initially presented at age 61 with diarrhoea, flatulence, anergia and weight loss: a jejunal biopsy revealed subtotal villous atrophy and she was commenced on a gluten free diet with good symptomatic effect. Repeat biopsy after 14 months still showed subtotal villous atrophy, and around that time her condition deteriorated with recurrence of diarrhoea, weight loss and development of ascites. Abdominal CT scan revealed lymphadenopathy which was confirmed on laparotomy. She died following acute occlusion of a leg artery.

## DISCUSSION

Gastrointestinal symptoms predominate in the initial presentation of coeliac disease. Diarrhoea/steatorrhoea was the commonest presenting complaint noted by Barry, Baker and Read<sup>2</sup> but the incidence in our population (56%) was considerably lower. Other authors have found between 74% and 97% of their patients to have diarrhoea or steatorrhoea.<sup>3,4,5</sup> Barry, Baker and Read commented on the fact that diarrhoea is less common as a presenting complaint in the adult

population but we found it consistently in our various age groups. Gastrointestinal symptoms accounted for 95% of presenting complaints in the 20–39 year age group, but only 60% of the 0–19 year age group. The other age groups were intermediate.

In our population 15% gave constipation as a presenting complaint, leaving 29% without any symptoms of altered bowel habit. Constipation has been reported as a presenting complaint in childhood coeliac disease, in 12 out of 112 children, nine of whom had faecal impaction.<sup>6</sup> In our study constipation occurred in all age groups.

Abdominal pain was the second most frequent complaint, especially in the 20–39 group, which also contrasts with one previous report,<sup>2</sup> although others found up to 42% of patients with this symptom.<sup>5</sup>

Jejunal biopsy is a safe diagnostic investigation. The indications for biopsy depend mainly on clinical, haematological and biochemical abnormalities. The correlation between these parameters and disease activity is of practical importance, but in our study an abnormally low haemoglobin was detected in only 45%, an abnormal serum folate in 39% and a low albumin in only 42% of patients. The Belfast study also indicated the need for caution in allowing a normal blood test to allay a clinical suspicion of malabsorption.<sup>5</sup>

Serum albumin concentration was below 35 g/dl in only 14% of patients. In a western population on a normal diet, values of less than 40 g/dl would be a more reasonable index of hypoalbuminaemia,<sup>6</sup> and 42% of our patients were below this level. Benson and his colleagues detected hypoproteinaemia in 73% of patients.<sup>3</sup>

On review of those claiming adherence to diet and complete remission of symptoms, and who had repeat biopsies, 78% had normal villi; in those claiming improvement but not full remission only 36% had a normal villous pattern. All those not adhering to diet but claiming improvement had subtotal or partial villous atrophy on repeat biopsy. Return to a normal villous pattern correlated well with complete remission of symptoms in patients on diet, but not in those who only had improvement in symptoms. A normal villous pattern did not occur in patients not adhering to diet.

Nineteen (17.8%) of our patients were first degree relatives. Selection bias would account for this figure which is higher than the previously recorded risk of coeliac disease among first degree relatives: 10.3% from the West of Ireland,<sup>8</sup> 11.2% from England<sup>9</sup> and 11.5% from America.<sup>10</sup>

Five of our patients died; only two from malignancy, one being a lymphoma. Most previous studies show a high incidence of lymphoma and carcinoma in coeliac patients. Brandt *et al*<sup>11</sup> found five cases of intestinal lymphoma in 74 patients; Holmes *et al*<sup>12</sup> found 28 malignancies in 210 patients, 22 being either lymphoma or carcinoma of the gastrointestinal tract. The average age at diagnosis of coeliac disease in these lymphoma patients was 53 years,<sup>12</sup> whereas 95% of our patients were under 60 years and 76% under 40 years at the time of diagnosis. In the study by Holmes and his colleagues<sup>12</sup> the duration from diagnosis of coeliac disease to lymphoma averaged 26 years, and averaged 25 years from diagnosis to carcinoma. Longer follow up and advancing age in the present group of patients may well result in an increased incidence of malignancy.

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