Juvenile onset inflammatory bowel disease: height and body mass index in adult life

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Abstract

Objective—To establish the frequency of permanent growth failure in juvenile onset inflammatory bowel disease.

Design—Measurement of height and weight in a geographically based cohort at a mean of 14 (range 5.2–29.5) years after diagnosis. Comparison with data from surveys of British adults in 1980 and 1987.

Setting—NHS hospitals throughout Scotland.

Subjects—105 Children admitted to hospital during 1968–83 who fulfilled diagnostic criteria for Crohn's disease or ulcerative colitis and lived in specified regions. 87 were aged over 18 and living in Britain at follow up.

Main outcome measures—Height, weight, body mass index, and sexual maturity.

Results—All patients were sexually mature. 67 of the 70 patients examined were of normal height, and three women with Crohn's disease were abnormally short. Weight and body mass index were normal in all patients with ulcerative colitis. Patients with Crohn's disease had significantly lower weight than those with ulcerative colitis (men 66.8 (9.5) kg *v* 78.4 (13.8) kg, $P=0.04$; women 51.5 (8.2) kg *v* 63.0 (12.1) kg, $P<0.02$) irrespective of disease activity. Body mass index was also significantly lower than the normal distribution ($P<0.01$). Growth retardation was not mentioned as a problem for any of the 17 patients interviewed only by telephone.

Conclusions—Despite growth retardation in the teenage years most young people with inflammatory bowel disease will eventually achieve normal height. Reasons for lower weight in patients with Crohn's disease remain to be established.

Introduction

A study of a geographically based sample of 105 patients with juvenile onset inflammatory bowel disease identified through the Scottish hospitals inpatients statistics system confirmed previous reports of high early morbidity.^{1,5} Many children with Crohn's disease were short and underweight for their age, and no improvement was found between diagnosis and follow up a mean of 7.2 years later.² Girls were more likely to be underweight than boys. In contrast, the height and weight centiles were normal in children with ulcerative colitis.² A further review of this series of patients has been undertaken to establish their health in young adult life.^{6,7} We report here data on height and weight.

Subjects and methods

Our original sample of 105 patients comprised patients admitted to Scottish NHS hospitals between 1968 and 1983. Criteria for inclusion were a diagnosis of Crohn's disease (ICD 555.0–555.9) or ulcerative

colitis (ICD 556.0); fulfilment of diagnostic criteria for Crohn's disease or ulcerative colitis; development of symptoms of inflammatory bowel disease before the age of 17; resident in Lothian (mainly urban) or Highland (rural) regions or, for Crohn's disease only, being in a 10% sample of cases from the rest of Scotland.² Subgroup analyses showed no differences between the 10% sample and the Lothian and Highland subgroups, and all data were combined.

We traced patients through hospital records, parents, general practitioners, and NHS regional records. With the agreement of the hospital consultant or general practitioner we wrote to patients and invited them to attend for clinical assessment. We evaluated the current health of those unwilling to attend by a telephone interview with either the patient or a parent. The protocol was approved by the Lothian medicine and clinical oncology ethics of research subcommittee.

Full details of the clinical assessments have been reported.⁶ We calculated the Crohn's disease activity index⁸ for patients with Crohn's disease and ulcerative colitis using a symptom diary completed by the patients for the seven days before the interview. In patients who had a stoma (15 with Crohn's disease, seven with ulcerative colitis) the number of loose stools was taken as the number of times the patient emptied liquid faeces from the ileostomy bag.

Clinical examination included assessment of pubertal status and measurements of height and weight. To measure height we asked patients to stand, bare feet together, with the back of their heels against a wall, head forward, and chin tilted so that their eyes were level with their ears. We then measured them with a wall mounted ruler.

Values for heights and weights of British men and women aged 20–34 years and for percentage distribution of body mass index in Scottish men and women were obtained from an extensive survey carried out in 1980.⁹ More recent values were also taken from a smaller survey conducted in 1987.¹⁰ Body mass index was calculated as weight (kg)/(height (m))².

Data are presented throughout as mean plus 1 SD. We used the two tailed *t* test to compare patients with Crohn's disease and ulcerative colitis. Analysis of variance was used to compare distribution of body mass index in our patients with that in the general population.

Results

Of the original cohort of 105 patients with inflammatory bowel disease, six had died, seven had emigrated, four were still children, and one did not, in retrospect, fulfil age criteria for the study. The remaining 87 were all traced and were alive in January 1991. We examined 70 patients (50 with Crohn's disease, 20 with ulcerative colitis) and made telephone

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TABLE I—Demographic and clinical details of patients with inflammatory bowel disease who were examined or interviewed by telephone

	Crohn's disease		Ulcerative colitis	
	Clinical assessment	Telephone contact	Clinical assessment	Telephone contact
No of patients	50	10	20	7
Males:females	28:22	3:7	9:11	5:2
Year of birth (range)	1953-70	1960-73	1952-72	1959-67
Year of onset (range)	1960-83	1976-83	1967-82	1974-83
Disease distribution at onset:				
Orofacial	2	1	NA	NA
Small bowel	14	3	NA	NA
Small bowel and colon	22	4	NA	NA
Colon	12	2	NA	NA
Rectal	NA	NA	2	3
Left sided	NA	NA	3	3
Extensive or total	NA	NA	15	1
Length of follow up from onset (years):				
Mean (SD)	13.4 (4.8)	10.0 (2.5)	14.6 (5.5)	8.4 (3.5)
Range	6.1-29.5	4.7-13.8	5.2-23.1	5.4-15.3
No of days in hospital:				
Mean (SD)	102.5 (85.6)	122.8 (149.7)	93.4 (70.7)	65.4 (96.1)
Range	7-483	9-512	7-294	3-275
No of hospital admissions:				
Mean (SD)	6.6 (4.1)	5.2 (5.3)	6.4 (4.9)	3.2 (2.5)
Range	1-20	1-19	1-21	1-8
No who had > 1 major operations	39	4	10	2
No with permanent stoma	15	1	7	2
Patient's view of general health:				
Well	31	6	17	7
Reasonable	13	1	1	0
Ill	6	3	2	0

NA=Not applicable.

contact with the remaining 10 patients with Crohn's disease and seven with ulcerative colitis.

PATIENTS WHO HAD CLINICAL ASSESSMENT

Among the patients we examined, general morbidity, as reflected by hospital admissions, was similar for those with Crohn's disease (mean 6.6 admissions, 102 inpatient days) and those with ulcerative colitis (mean 6.4 admissions, 93 inpatient days) (table I) and for men and women. For Crohn's disease, the patients examined and those contacted only by telephone were very similar. For ulcerative colitis, however, the patients who declined to attend for clinical examination were predominantly men with less extensive disease and fewer hospital admissions (table I).⁶

Sixty eight of the 70 patients reported that their symptoms and general health at the time of the clinical interview reflected their clinical state for the previous six months or longer; one man with Crohn's disease had recently developed obstructive symptoms after a long remission, and one man had a recent relapse of ulcerative proctitis. One woman with Crohn's disease had intestinal failure and was receiving home total parenteral nutrition.

Figure 1 shows the Crohn's disease activity index for the patients. Ten of 22 women with Crohn's disease had an activity index above 150 compared with only six

of the 28 men ($P < 0.05$). The Crohn's disease activity index was above 150 in only two of the 20 patients with ulcerative colitis.

Table II and figures 2 and 3 show the heights and weights of patients with Crohn's disease and ulcerative colitis. The height of patients with Crohn's disease and ulcerative colitis was similar to that of normal adults, and we found no difference between patients with Crohn's disease and ulcerative colitis or men and women ($P > 0.1$), although there were three abnormally short women with Crohn's disease. The weight of men ($P = 0.04$) and women ($P < 0.02$), with Crohn's disease was significantly lower than that of those with ulcerative colitis.

The three short women had no specific common features. One woman (height 1.41 m), aged 27 at follow up, had developed orofacial and anal Crohn's disease at age 10; she had had no surgery and her only recent symptoms were mouth lesions. At the time of her clinical assessment she weighed 63 kg. Another 27 year old woman (height 1.44 m, weight 43.4 kg) had had Crohn's disease since the age of 12. It was complicated by duodenal ulceration with duodenal stenosis, and she had had four laparotomies with appendicectomy, three small bowel resections, vagotomy, and gastro-enterostomy. She was the most seriously ill patient in the series and received home total parenteral nutrition. The third patient (height 1.45 m, weight 33.6 kg) had developed small bowel and anal Crohn's disease at age 10. She was 19 years old at the time of the assessment and had recently had pan-proctocolectomy. Her height

FIG 1—Crohn's disease activity index at mean of 14 years after diagnosis in 50 patients with juvenile onset Crohn's disease and 20 with juvenile onset ulcerative colitis

TABLE II—Data on height and weight for Scottish men and women with juvenile onset inflammatory bowel disease and for normal British population in same age group^{9,10}

	Height (m)			Weight (kg)		
	No of patients or subjects	Mean (SD)	Range	No of patients or subjects	Mean (SD)	Range
Men:						
Crohn's disease	28	1.75 (0.09)	1.63-1.90	28	66.80 (9.5)	47.7-84.7
Ulcerative colitis	9	1.75 (0.10)	1.60-1.90	9	78.4 (13.8)	59.0-100.0
British population						
20-24 in 1980 ⁹	537	1.76		518	71.4	
25-29 in 1980 ⁹	557	1.75		539	73.0	
30-34 in 1980 ⁹	541	1.75		523	74.9	
25-34 in 1987 ¹⁰	269	1.76	1.65-1.88*	279	76.3	59.6-98.0*
Women:						
Crohn's disease	22	1.57 (0.07)	1.41-1.71	22	51.5 (8.2)	33.0-63.0
Ulcerative colitis	11	1.59 (0.06)	1.49-1.65	11	63.0 (12.1)	48.5-85.9
British population						
20-24 in 1980 ⁹	582	1.62		548	59.2	
25-29 in 1980 ⁹	576	1.62		560	59.2	
30-34 in 1980 ⁹	583	1.62		561	61.2	
25-34 in 1987 ¹⁰	261	1.63	1.53-1.73*	267	63.2	47.8-92.4*

*5th-95th Centile.

FIG 2—Height at clinical review in early adult life (mean 14 years after diagnosis) for 50 patients with juvenile onset Crohn's disease and 20 with juvenile onset ulcerative colitis. Relative distributions of height for British men and women in same age group are also shown

did not increase during a further two years of follow up.

Table III shows the distribution of body mass index. Distribution of body mass index was similar to that of the normal population in men and women with ulcerative colitis but significantly skewed towards low values for body mass index in those with Crohn's disease ($P < 0.01$).

Although relative weight for height is a factor used to calculate the Crohn's disease activity index,⁸ low body mass index was not related to disease activity. Among patients with Crohn's disease, body mass index ranged from 14.9 to 27.1 in men with active disease; from 16 to 25.6 in men with inactive disease; from 16 to 24.7 in women with active disease; and from 13.1 to 31.7 in women with inactive disease.

Limited information on previous treatments had been collected, and we could not estimate lifetime doses of drugs. Systemic corticosteroids had been taken at some time by 19 of 28 men and 16 of 22 women with Crohn's disease (only one of the three short women) and by five of nine men and seven of 11 women with ulcerative colitis. At the time of assessment seven patients with Crohn's disease and one with ulcerative colitis were taking oral prednisolone 5-15 mg/day.

Four patients with ulcerative colitis were obese. Corticosteroid treatment for chronically active disease may have contributed to this in a woman who weighed

85 kg, but the three men who weighed over 85 kg had never taken steroids.

INFORMATION ON PATIENTS INTERVIEWED BY TELEPHONE

Documentation of height and weight in the case records was poor.⁷ When we made telephone contact with the 17 patients who did not attend for interview we asked about general health and wellbeing but not about height. Two patients with Crohn's disease, a man and a woman, had chronic ill health. They had spent long periods in hospital and were being considered for home total parenteral nutrition. No patient or parent indicated short stature was a problem, and permanent growth retardation was not mentioned in the hospital records of any patient. Of the seven women with Crohn's disease, one was 1.54 m at age 14 and two were normal height as adults (1.63 m and 1.65 m); height was recorded for one of the three men with Crohn's disease (1.72 m). No data on heights were available for the five men and two women with ulcerative colitis.

FIG 3—Weight at clinical review in early adult life (mean 14 years after diagnosis) for 50 patients with juvenile onset Crohn's disease and 20 with juvenile onset ulcerative colitis. Relative distributions of weight for British men and women in same age group are also shown

SEXUAL DEVELOPMENT

Records of growth and development were incomplete, and we did not attempt to assess the timings of growth spurt or the stages of puberty. However, when asked if they had developed at the same time as their peers, 11 of the 28 men with Crohn's disease and 13 of the 22 women reported delayed development; for ulcerative colitis the figures were two of nine men and three of 11 women.⁶ Differences between patients with Crohn's disease and ulcerative colitis were not significant. All patients had normal external genitalia, but vaginal examination was not done.

The age at menarche was similar to that of the general population in women in the ulcerative colitis group, but several women with Crohn's disease who had not menstruated before the onset of symptoms reported considerably delayed menarche (fig 4).

Discussion

Reports of growth and development in young people with inflammatory bowel disease consistently record retardation of sexual maturation and of growth.¹¹ Reduced growth has been recognised even before the onset of symptoms,¹² and growth spurts after surgery

TABLE III—Distribution of body mass index in Scottish men and women and in patients with juvenile onset inflammatory bowel disease. Figures are numbers (percentages)

	Scottish population aged 16-64 in 1980 (%) ⁹	British population aged 25-34 in 1987 (%) ¹⁰	Crohn's disease	Ulcerative colitis
Men:				
No of people	397	269	28	9
Body mass index:				
≤20	9	4	9 (32)	
-25	54	60	15 (54)	6 (67)
-30	33	30	4 (14)	1 (11)
-35	5	6		1 (11)
-40				1 (11)
Women:				
No of people	453	261	22	11
Body mass index:				
≤20	15	17	7 (32)	1 (9)
-25	56	56	14 (64)	5 (45)
-30	22	16		3 (27)
-35	6	11	1 (4)	2 (19)
-40	1	1

FIG 4—Age at menarche in 22 women with juvenile onset Crohn's disease and 11 with juvenile onset ulcerative colitis according to timing of onset of symptoms of inflammatory bowel disease

may be transient and unpredictable.¹³⁻¹⁶ Crohn's disease and ulcerative colitis cases are not differentiated in all reports, but generally it is accepted that growth delay is less of a problem in ulcerative colitis than Crohn's disease.

Recent follow up data for several series of children with Crohn's disease have shown that although successful treatment may lead to resumption of linear growth rates, catching up in the teenage years is unusual.^{2,17,18} Many patients in these series, however, were still teenagers at the end of the study period, although it seems likely that some of them will be abnormally short in adult life.

Sixty seven of the 70 patients we examined ultimately achieved a normal adult height. There were no common features in the three patients with permanent short stature, apart from being female and having Crohn's disease. Of the remaining 10 patients with Crohn's disease in the original cohort, four are known to be of normal height and for the others no comments on abnormal stature have been found in hospital records or in our contacts with them or their relatives.

The patients with ulcerative colitis whom we examined had normal weight and body mass index, but weight and body mass index were lower than in the general population in men and women with Crohn's disease. Body mass index and Crohn's disease activity index were not significantly associated.

AMERICAN FINDINGS

A study in America reported permanent impairment of growth in 14 of 38 (37%) patients with Crohn's disease and one of 10 with ulcerative colitis.¹⁹ The heights were judged in relation to American population

norms (mean SD 1.725 (0.062)m for men; 1.639 (0.073)m for women), which are similar to published normal values for British adults and values in our patients. The heights of the New York patients with growth failure (men 1.649 (0.06)m; women 1.48 (0.096)m) were clearly shorter than those of our patients.

Patients in the American and our series had similar clinical features such as age at onset and disease distribution. Our series was a geographically based sample, and patients were treated by many paediatricians, gastroenterologists, and surgeons whereas the American series was from a single specialist centre and may reflect a degree of referral bias. The most striking differences between the two series, however, was in the management strategies. The 15 American patients with impaired growth (14 with Crohn's disease) had a high rate of treatment with oral or intravenous nutritional supplementation (50%), oral corticosteroids (85%), and mercaptopurine or azathioprine (60%) and relatively low rates of surgery (38%). In our series more patients had had surgical treatment (57% at 7.2 year follow up, 78% at 14 years) and fewer had had second line medical treatment (72% oral corticosteroids, 18% azathioprine, 24% nutritional therapy).⁶

MECHANISMS OF GROWTH RETARDATION

The mechanisms which cause growth delay and pubertal arrest in teenagers may also cause low weight, irrespective of disease activity, in adults with Crohn's disease. Possible factors include growth hormone deficiency, impaired metabolic responses to growth hormone, low intake of energy and specific nutrients, loss of protein and blood through the gut, and increased metabolic rate.¹¹ Resting metabolic rate and total daily energy expenditure were reported to be normal in patients with stable inflammatory bowel disease,²⁰ and growth retarded children with inflammatory bowel disease generally have normal growth hormone responses.²¹ These patients, however, have low concentrations of insulin-like growth factor 1,²² and this has also been reported in malnourished adults with inflammatory bowel disease.²³

As intensive nutritional replacement can reverse growth failure, malnutrition is thought to be an important factor in growth retarded children with Crohn's disease.²⁴ Investigation of malnutrition in adults will require careful recording not only of energy and nutrient intake and absorptive capacity but also of patterns of eating, appetite, and feeding behaviour. There are many potential approaches to the prevention and treatment of low weight in patients with inflammatory bowel disease, including nutritional therapy, immunosuppression, immunomodulation, exercise programmes, endocrine treatment, and intervention with appetite stimulants. Adults with ulcerative colitis who have normal weight and height might provide useful controls for comparisons with patients with low weight and low body mass index in future studies.

When a chronic and essentially incurable disease is diagnosed in a child, many issues of prognosis and likely morbidity are raised. Parents of children with inflammatory bowel disease can be reassured that adult height and sexual development will usually be normal.

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Clinical implications

- Growth retardation is common in children with inflammatory bowel disease, particularly Crohn's disease
- In this study 67 of 70 children with Crohn's disease or ulcerative colitis were of normal height as adults, mean of 14 years after onset of disease
- Patients with Crohn's disease had significantly lower weight than the normal population
- All patients were sexually mature
- Children and teenagers with inflammatory bowel disease should have height and weight measured regularly and sexual development recorded

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Alcohol and blood pressure: the INTERSALT study

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Abstract

Objectives—To assess the relation between alcohol intake and blood pressure in men and women and in men at younger and older ages; to examine the influence of amount and pattern of alcohol consumption, as well as of acute effects, taking into account body mass index, smoking, and urinary sodium and potassium excretion.

Design—Subjects reported alcohol consumption for each of seven days before standardised blood pressure measurement, and whether they had consumed any alcohol in the 24 hours before measurement.

Setting—50 centres worldwide.

Subjects—4844 men and 4837 women aged 20-59.

Main outcome measures—Effect of alcohol on blood pressure estimated by taking a weighted average of regression coefficients from centres. Acute effect assessed by examining mean differences in blood pressure of non-drinkers and of heavy drinkers who had and had not consumed alcohol in the 24 hours before measurement. Effect of pattern of consumption assessed by examining mean differences in blood pressure of non-drinkers compared with drinkers (i) whose intake was concentrated in fewer days or who were drinking more frequently, and (ii) whose alcohol intake varied little over the seven days or varied more substantially, as indicated by the standard deviation of daily consumption.

Results—Of the 48 centres in which some people reported consuming at least 300 ml/week of alcohol, 35 had positive regression coefficients linking heavy alcohol consumption to blood pressure. Overall, alcohol consumption was associated with blood pressure, significantly at the highest intake. After account was taken of key confounders, men who drank 300-499 ml alcohol/week had systolic/diastolic blood pressure on average 2.7/1.6 mmHg higher than non-drinkers, and men who drank ≥ 500 ml

alcohol/week had pressures of 4.6/3.0 mmHg higher. For women, heavy drinkers (≥ 300 ml/week) had blood pressures higher by 3.9/3.1 mmHg than non-drinkers. Heavy drinking and blood pressure were strongly associated in both sexes, and in men at both younger (20-39 years) and older (40-59 years) ages. In men who were heavy drinkers, episodic drinkers (those with great variation in daily alcohol consumption) had greater differences in blood pressure compared with non-drinkers than did regular drinkers of relatively constant amounts.

Conclusion—The significant relation of heavy drinking (3-4 or more drinks/day) to blood pressure, observed in both men and women, and in younger and older men, was independent of and added to the effect on blood pressure of body mass index and urinary excretion of sodium and potassium. The findings indicate the usefulness of targeting those at high risk as well as the general population to reduce the adverse effects of alcohol on blood pressure.

Introduction

INTERSalt, an international multicentre epidemiological study,^{1,2} earlier reported significant associations of urinary sodium excretion and body mass index (direct), and urinary potassium excretion (inverse) with blood pressure.^{3,4} The study showed, in addition, that consumption of 300 ml of alcohol per week (three or four drinks a day) or more was directly related to higher blood pressure of individuals. In two of the 52 centres in the study, the Yanomamo and Xingu Indians of Brazil, no alcohol was consumed. This report uses data on 9681 men and women from the remaining 50 centres to examine the relation between amount of alcohol consumed and blood pressure in men and women separately, and in younger and older men, independent of the effects of body mass index, smoking, and urinary excretion of sodium and potassium.