Ulcerative colitis in Asian immigrants

G.F.A. Benfield, R.D. Montgomery and P. Asquith

Department of Gastroenterology, East Birmingham Hospital, Bordesley Green East, Birmingham B9 5ST, UK.

Summary: Forty-four Asian immigrants in Birmingham and 44 age- and sex-matched white Caucasians with ulcerative colitis were compared to investigate the existence of any ethnic differences in the pattern of disease. Asian immigrants demonstrated a male preponderance of 2:1, and compared to the matched Caucasians there was a higher incidence of presenting eosinophilia and a milder course of disease, with more patients experiencing only a single initial attack. In spite of this clinical difference, total or subtotal colitis was the commonest pathological type in both white Caucasians and Indians, whereas in Pakistanis localized distal disease predominated. All ethnic groups suffered the same overall complication rate (55%) which is at variance with the experience of low complication rates in India. The age of onset of ulcerative colitis was related to age at immigration with a mean interval of 11 years.

Although in some respects Asian immigrants share the disease pattern of the indigenous population, the observed significant differences could be of importance with regard to pathogenesis.

Introduction

Ulcerative colitis (UC) has been extensively investigated within populations indigenous to the Western hemisphere, including Britain.^{1–3} Little was known of the prevalence and behaviour of this disorder in other ethnic groups until relatively recently, when several studies confirmed that UC is widespread in India but suggested the existence of differences in disease pattern compared to that in Western countries.^{4–7}

In Britain there has been an established Asian population (Indian and Pakistani) of increasing proportions for over 20 years, in whom details of the behaviour of UC is sparse.⁸ A recent study indicated that the prevalence of the disease is similar to that of the indigenous population.⁹ It has been suggested that environmental influences, at present undefined, play a part in the pathogenesis of the disease and may be relevant in groups, such as Asian immigrants, who move from rural to urban areas.¹⁰ Thus it is important to establish any subtle differences in the pattern of UC in Asian immigrants which could relate to ethnic or cultural factors. We have reviewed our experience of such patients over a 16-year period in a hospital covering a city with a large immigrant population.

Patients and methods

The clinical and radiological records of all 44 Asians with UC referred during the period 1968–84 were reviewed. These were obtained via the computer-based Hospital Activities Analysis (HAA) which recorded all

in- and out-patients who had attended East Birmingham Hospital with an established diagnosis of UC. Using these details the Asian patients were matched for age (± 3 years) and sex with white Caucasian patients randomly allocated on an age band basis from the HAA list. The patients were drawn from throughout the Birmingham health district. Population figures for Indian and Pakistani immigrants in Birmingham were obtained from the National Census survey of 1981.¹¹

The diagnosis of UC was based on a compatible history, sigmoidoscopic appearances, rectal biopsies and barium enema examination. In four Asians and seven white Caucasians supplementary histology was provided by resected colon, and in 15 Asians and 19 white Caucasians radiology was supplemented by flexible colonoscopy. Infective colitis was rigorously investigated and excluded. Fresh stool specimens were examined by microscopy for ova, cysts and parasites and cultured for *Mycobacterium tuberculosis*, *Salmonella* and *Shigella* spp., *Campylobacter jejuni* and *Yersinia enterocolitica*. Blood investigations included Widal titrations for *S. typhi* and *paratyphi*, and fluorescent antibody tests for *Entamoeba histolytica* and *Schistosoma mansoni*.

From the Asian patients the following details were obtained: age at immigration, years in Britain before the onset of symptoms and age at onset of UC. From all records the following details at presentation were extracted: haemoglobin (Hb), total and differential white cell count (WBC), serum albumin, orosomucoid and erythrocyte sedimentation rate (ESR). The extent of disease was determined following sigmoidoscopy and subsequent colonoscopy and/or large bowel

Correspondence: G.F.A. Benfield, M.B., M.R.C.P.

Accepted: 2 March 1987

radiology. Patients were classified as having either distal colitis (proctitis or procto-sigmoiditis), left sided colitis (disease distal to mid-transverse colon) or total/sub-total (disease proximal to mid-transverse colon).

Details of maintenance treatment and the subsequent course of disease including complications, length of follow-up, surgery and deaths were also extracted. The pattern of disease in patients during follow-up was defined as either single episode (clinical remission following the presenting active episode), relapse-remitting (alternating periods of disease activity and quiescence) or chronic continuous (varying degrees of persistently active disease). Because of the possibility of acute self-limiting colitis (ASLC) being erroneously diagnosed as UC, patients were excluded who presented with a single episode of colitis and who subsequently demonstrated no clinical, radiological or colonoscopic features of UC and who had normal bowel histology.

Initial treatment consisted of oral sulphasalazine and/or corticosteroids depending on the severity of the attack. Maintenance treatment consisted of oral sulphasalazine in all patients supplemented when necessary by rectal steroid enemas for troublesome local symptoms. Relapses of UC were treated with systemic corticosteroids and/or an increased dose of sulphasalazine. Use was often made of low-milk or milk-free diets.

Statistical analysis

Information was analysed using Student's paired or unpaired *t*-test for parametric data and chi-squared tables with Yate's correction for non-parametric data.

Figure 1 Age at onset of symptoms in Asian immigrants compared to the first generation immigrant population overall. Numbers of patients within age bands expressed as percentages. ■, First generation immigrants; □, first generation patients with ulcerative colitis.

Where appropriate, non-parametric data was analysed in multiway frequency tables utilizing the log-linear model. Probability figures of >0.05 were regarded as non-significant (NS).

Results

Sex ratio

The 44 Asian patients (Indian 23, Pakistani 21) included 29 males giving a male:female ratio of 2:1. Population figures for Birmingham in 1981 indicate that the Indian and Pakistani (excluding Bangladeshi) males totalled 25848 and the females 21351, giving a male:female ratio of 1.2:1. Mid-year predictions based on the 1981 census indicate that these ratios have not altered significantly.

All but three patients were first-generation immigrants with two having developed symptoms of UC prior to their arrival in Britain.

Age

The age distribution at the onset of symptoms in Asian immigrants is shown in Figure 1 and generally reflects the Asian population of Birmingham. The mean (± 1 s.d.) age of onset of Asian immigrants overall was 32.2 ± 12.9 years with males (34.9 ± 12.9 years) developing symptoms later than females (27.1 ± 11.8 years, $P = 0.05$). The matched white Caucasians had a mean age of onset of 33.0 ± 13.3 years.

In both sexes there was a close correlation between the age of immigration and the onset of UC (Figure 2),

Figure 2 Relation of the age at immigration to Britain to the eventual age at which symptoms developed; $n = 39$, $r = 0.83$, $P < 0.001$.

Table I Summary of laboratory investigations reflecting disease activity at presentation of 44 patients of each ethnic group with ulcerative colitis (mean $\pm$ 1 s.d.).

	Asians	White Caucasians	<i>t</i>	<i>P</i> value
Haemoglobin (g/dl)	12.4 $\pm$ 2.4	11.4 $\pm$ 2.4	1.90	NS
Albumin (g/l)	34 $\pm$ 8	33 $\pm$ 7	0.76	NS
Orosomucoid (g/l)	1.42 $\pm$ 0.62	2.0 $\pm$ 0.78	- 3.41	0.001
White cell count ($\times 10^9$ /l)	9.1 $\pm$ 3.6	10.3 $\pm$ 3.4	- 1.68	NS
Differential				
Normal	19	21		
Neutrophilia	6	20		
Eosinophilia	19	3	$\chi^2 = 19.3$,	< 0.001

NS = not significant

the mean ($\pm$ 1 s.d.) age at immigration being 22.8 $\pm$ 11.5 years and the age at onset being 33.6 $\pm$ 12.2 years. Sixteen (39%) first-generation immigrants developed symptoms 8–12 years after immigration and 29 (71%) did so 6–16 years after arrival in Britain. Only two patients suffered symptoms within 5 years of immigration.

Laboratory investigations

Table I summarizes the haematological and biochemical parameters of disease activity at presentation. The serological results revealed no difference between Asians and white Caucasians apart from the serum orosomucoid which was higher in the latter group. This difference was attributable to the patients with left-sided colitis (2.11 $\pm$ 0.85 vs 1.38 $\pm$ 0.47 g/l, $P < 0.05$) and total colitis (2.1 $\pm$ 0.70 vs 1.59 $\pm$ 0.67 g/l, $P < 0.05$).

Haematological measurements indicated that eosinophilia (eosinophil count $> 0.44 \times 10^9$ /l) was frequent in Asian immigrants with 19 (43%) patients demonstrating this feature at presentation. In contrast only four white Caucasians had an initial eosinophilia and in three of these active allergic disorders were present. The presence of eosinophilia at presentation was not related to the extent or course of the colitis, parasitic infestation or the presence of atopic disorders.¹²

Extent of disease

The extent of colonic involvement in Indian patients matched that of the white Caucasians (Table II). In contrast distal disease predominated in Pakistani patients, the differences being statistically significant in spite of small numbers ($\chi^2 = 6.84$, $P < 0.01$).

Course of disease and complications

The subsequent course of disease during treatment and follow-up differed significantly between the two groups (Table III) with 50% of Asian patients experiencing continued remission after the initial episode whereas 77% of white Caucasians suffered a relapsing pattern ($\chi^2 = 10.69$, $P < 0.005$). In neither group did the course of disease correlate with the extent of colonic involvement ($\chi^2 = 4.66$ and 2.05 respectively, $P = \text{NS}$). In patients with only a single episode of active disease the diagnosis of UC (in contrast to ASLC) was confirmed by subsequent rectal/colonic biopsies obtained from one month to 5 years after the initial presentation, histological examination of which demonstrated persisting abnormalities consistent with chronic inflammation. Such biopsies were undertaken in 16/22 affected Asians, the remaining 6 patients demonstrating UC radiologically at 1–5 months from discharge. Similarly, later biop-

Table II Degree of colonic involvement determined by sigmoidoscopy plus barium enema examination and/or colonoscopy

	Distal	Extent of disease		
		Left-sided colitis	Total/ sub-total	
Indian	4	6	13	$\chi^2 = 6.84$, $P < 0.01$
Pakistani	9	5	7	
Total	13	11	20	
White Caucasians	8	11	25	$\chi^2 = 1.75$, $P = \text{NS}$

Table III Course of disease and relationship with extent of colonic involvement following institution of treatment and out-patient attendance.

	<i>Course of disease</i>		
	<i>Single episode</i>	<i>Relapse-remitting</i>	<i>Chronic-continuous</i>
Asians			
Distal colitis	6	7	0
Left-sided colitis	7	4	0
Total/sub-tot. colitis	9	8	3
	22	19	3
White Caucasians			
Distal colitis	2	6	0
Left-sided colitis	1	10	0
Total/sub-tot. colitis	6	18	1
	9	34	1

sies were obtained in 6/9 white Caucasians, a further 2 showed UC radiologically despite being asymptomatic at follow-up, and 1 patient presented with a 4-month history.

Complications occurred in 24 (55%) patients from

both groups (Table IV), four Asians and five white Caucasians having anaemia as the sole complication. Local bowel complications arose in 13.6% of Asian immigrants and 22.7% of white Caucasians and systemic complications in respectively 52.3% and

Table IV Local and systemic complications arising during the course of ulcerative colitis

	<i>Asians</i> (24/44)	<i>White Caucasians</i> (24/44)
<i>Local:</i>	<i>n = 6</i>	<i>n = 10</i>
Acute colonic dilation	3	1
Anal fistula	1	—
Pseudopolyps	3	5
Polyps	—	3
Rectal prolapse	1	—
Haemorrhoids	—	2
Carcinoma of colon	—	1
<i>Systemic</i>	<i>n = 23</i>	<i>n = 20</i>
Anaemia (<10 g/dl)	11	11
Oral ulcers	4	4
Arthritis	5	3
Cutaneous	2	3
Ocular	1	—
Clubbing	2	1
Cirrhosis	1	1
Non-specific hepatitis	1	—
Sclerosing cholangitis	—	1
Chronic pancreatitis	—	1
Myeloma	1	—
Glomerulonephritis	1	—
Drug toxicity	—	1
Surgery	4	7
Deaths	4	3

Table V Details of follow-up period and reasons for non-attendance

	Asians	White Caucasians	
Period of follow-up (years, mean $\pm$ 1 s.d.)	3.2 $\pm$ 2.5	6.3 $\pm$ 4.3	$t = -4.1, P < 0.001$
Median (years)	3.1	4.5	
Range (years)	0.25 – 11.3	0.2 – 16.6	
Currently under follow-up	23	36	$\chi^2 = 8.74, P < 0.05$
Lost to follow-up	19	7	
Died during follow-up	2	1	
Reasons for non-attendance:			
Emigration	13	0	
Moved area	4	1	
Unknown	2	6	

45%. The nature of the complications was similar in the two groups, with the possible exception of pseudopolyp and polyp formation.

Four Asians and seven white Caucasians underwent a panproctocolectomy for severe colitis. Four deaths occurred in the Asian group; two were post-operative, one from myeloma¹³ and one from bleeding oesophageal varices due to cirrhosis following chronic active hepatitis. Of the three deaths in the white group one was post-operative, one due to ischaemic heart disease and one due to colonic carcinoma.

Follow-up of patients

Details of follow-up are summarized in Table V. White Caucasians attended hospital for a longer period than did Asians with fewer being lost from supervision ($\chi^2 = 8.74, P < 0.05$). The seven patients lost in the white Caucasian group were due to moving area or default from follow-up but the predominant reason in the Asian group was emigration. Although

those Asians lost were followed up for a shorter period overall than those currently under follow-up (Table VI), their default was not, in contrast to the white Caucasian group, related to the course of disease; Asian patients with relapsing disease absented themselves as often as those with continued remission and the disease patterns were similar in those lost to, and currently under, follow-up.

Discussion

Uncontrolled studies from India have suggested that UC in the indigenous population is a milder disorder than that which occurs in Western populations, with a low incidence of local and particularly systemic complications.⁴⁻⁷ There have been no data on the presentation and follow-up of Asians moving from the Indian subcontinent to temperate zones. We have attempted to elucidate the pattern of behaviour of UC in Asians who have emigrated from predominantly rural villages

Table VI Effect of loss to follow-up on duration of hospital attendance and classification of the eventual course of disease.

	Single episode	Course of disease Relapse- remitting	Chronic- continuous
<i>Asians</i>			
Lost to follow-up (19)	10	9	0
Period of follow-up (years)	1.5 $\pm$ 1.0	3.7 $\pm$ 3.1	—
Current follow-up (23)	11	10	2
Period of follow-up (years)	3.8 $\pm$ 1.8	4.3 $\pm$ 2.8	—
<i>White Caucasians</i>			
Lost to follow-up (7)	5	2	0
Period of follow-up (years)	2.6 $\pm$ 1.3	—	—
Current follow-up (36)	4	31	0
Period of follow-up (years)	3.6 $\pm$ 0.9	7.5 $\pm$ 4.3	—

in the North-western region of the Indian subcontinent to a Western industrialized conurbation. The findings have been compared with a control group of concurrently observed indigenous white Caucasians also with UC.

The male:female ratio of UC in European studies is 1:1.3.^{14,15} Based on the Birmingham census figures the expected ratio for Indian and Pakistani patients should be 1:1, whereas the observed ratio was 2:1. This marked male preponderance is in keeping with studies in India. Our findings are likely to reflect the situation overall in Birmingham given the random drawing of patients from throughout the city.

The age of onset of symptoms of UC was closely related to the age at immigration, an interesting observation with alternative explanations. The results may simply reflect the population characteristics of the Asian population together with the peak incidence of UC which occurs between the third and fifth decades.^{1,14} If this were so a more random time of onset might have been expected. Alternatively, the temporal relationship between immigration and development of symptoms could imply a slow-acting environmental influence, particularly as only two patients developed symptoms within their first 5 years of residence and only two patients had symptoms prior to immigration.

A circulating eosinophilia was a significant finding in Asians presenting with untreated disease in the clear absence of parasitic infestation. This feature, which disappeared following treatment for UC, was not evident to any significant degree in the white Caucasians although an association has been suggested previously in studies of treated patients.^{16,17} In this instance the observed eosinophilia suggests either a racial difference in the response to UC or a difference in pathogenesis.¹² In the only Asian account which documents the white cell differential count no eosinophilia was detected at presentation.¹⁸

In both groups the extent of bowel involvement was similar. Comparisons between studies are unsatisfactory due to varying definitions of the degree of colonic involvement; nevertheless both Indians and Caucasians demonstrated a greater frequency of total or sub-total involvement (56% and 57% respectively) than has been reported in earlier surveys in Britain (22–34%)^{1,2} and in India (11–33%).^{4–7} Our findings may reflect improved radiological techniques and the increased use of fiberoptic endoscopy.¹⁹ Pakistani subjects on the other hand showed a significantly greater predominance of distal disease, the reasons for which are not readily apparent. The single survey from Pakistan¹⁸ reported distal colitis in 37.5% of patients and total colitis in 40.6%; the lack of histology and the apparent absence of left-sided colitis obscures the interpretation of these figures. Probably the most important difference between the two immigrant groups is their diet. The muslim Pakistanis for exam-

ple eat meat killed in the Hallal manner and Indians, mainly from villages in the north-west, change from drinking goat's milk to cows milk on emigrating to Britain. If dietary factors do play a part in UC²⁰ Asian immigrants would provide a good example of antigenic changes from this source.

A further difference between Asians and white Caucasians was in the clinical course of the disease. A single episode followed by a sustained remission was the predominant course in the former and relapse-remitting disease dominated the latter. Acute self-limiting colitis may be clinically indistinguishable from early UC thus resulting in an erroneous diagnosis of the latter. However certain features are typical of ASLC, namely: an acute diarrhoea, the isolation of bowel pathogens in 40% or more patients and a rapid complete resolution within approximately 4 weeks of presentation.^{21,22} Histologically there are few features specific for ASLC other than the absence of those regarded as characteristic for UC – distorted crypt architecture, crypt atrophy, a villous surface and possibly increased numbers of round cells and neutrophils.^{22,23} Further biopsies taken 3–4 weeks after the onset of symptoms reveal marked resolution of inflammation in ASLC^{21,24} whereas persisting abnormalities, including the aforementioned changes, virtually exclude the diagnosis.^{23,24} We are confident that in our patients with single-episode disease ASLC was excluded mainly because of long-standing histological changes consistent with UC, the remaining patients demonstrating clinical and radiological features unlike that of ASLC. It could be argued that the predominance of single episode disease must be viewed in the context of a shorter period of follow-up in Asian immigrants, with a higher rate of default which was mainly occasioned by return to their homeland. As we have shown, however, there was no selective loss of patients running a benign course, whereas, in contrast, default from follow-up in the white Caucasians was mainly due to absence of symptoms after the initial attack. The difference in clinical course between the two ethnic groups is therefore a valid finding, and the difference in levels of serum orosomucoid may be a reflection of this. It might seem paradoxical that in Indian patients the clinical course was more benign than in the Caucasians with the same degree of bowel involvement, but it is recognized that there is no clear correlation between these two parameters.²⁵

Our study has shown that the prevalence of both local and systemic complications was the same in Asians and white Caucasians (55% overall in both groups), and was comparable to that from other Western studies.^{26,27} The rarity of these complications in India and Pakistan has been reported from both South and North India⁶ and Pakistan¹⁸ and in spite of the obvious difficulties of achieving prolonged follow-up in these countries this difference is probably

genuine since the most severe and complicated cases are more likely to be seen in hospital. It is notable that a tendency to a milder clinical course and fewer complications has also been observed in a recent follow-up study of Arab patients with UC in Kuwait.²⁸

In short, UC in the two groups that we have studied is similar with regard to extent of bowel involvement and prevalence of local and systemic complications – the only exception being the less extensive disease in

Pakistanis. There are however distinctive features in the immigrant group, namely a high incidence of circulating eosinophilia in untreated disease, a male preponderance and a more benign course of disease overall. These last two features would seem to agree with reports from India, whereas in other respects the apparent change to a more Western pattern in immigrants suggests a shift in emphasis of unknown environmental rather than racial factors.

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