Epidemiology of Crohn's Disease in Indian Migrants and the Indigenous Population in Leicestershire

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SUMMARY

A retrospective, epidemiological community study of Crohn's disease was performed in Leicestershire from 1972 to 1989. The county population of 930,000 includes 93,000 South Asians. Potential cases were identified from hospital departments of pathology, endoscopy and medical records, in addition to general practitioners. There were 582 cases in Europeans and 28 in South Asians. The incidence of Crohn's disease in Europeans and South Asians has increased, particularly in Muslims. The standardized incidence in South Asians during the 1980s was $2.4/10^5/y$ ear in Hindus, $3.4/10^5/y$ ear in Sikhs and $5.4/10^5/y$ ear in Muslims. The standardized incidence in Europeans has risen significantly to $4.7/10^5/y$ ear from $3.4/10^5/y$ ear in the 1970s ($\chi^2 = 8.1$, p < 0.005). In Leicester this increase can be accounted for entirely by new cases of colonic disease. All ethnic groups had a similar disease distribution. Small bowel disease was inversely associated with age, whilst colonic disease increased with age. However, the difference in age-specific incidence of Crohn's disease for different age bands at various sites was not significant. Overall, Hindus have a much lower incidence of Crohn's disease than Europeans.

INTRODUCTION

Epidemiological studies have shown marked regional variations in the incidence of Crohn's disease [1-19]. Most studies have been performed in westernized countries [1-18]. There are few reliable data [19, 20], although it seems rare. The study of people who migrate from such areas of low incidence to those with high incidence, or *vice versa*, is a useful epidemiological tool in evaluation of aetiological factors. The few British studies of inflammatory bowel disease in people whose families originated in the Indian Subcontinent (South Asians) [21, 22] suggest the incidence of Crohn's disease is lower than in Europeans [23, 24].

Leicester is in the East Midlands and has a large textile industry. Substantial immigration occurred in the 1960s and early 1970s from South Asia and East Africa. Most migrants were

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Gujarati Hindus (80 per cent) and Punjabi Sikhs (12 per cent) [25], although there were also a number of South Asian Muslims.

The aim of this study was to determine the incidence of Crohn's disease in Leicestershire and compare incidence in South Asians and Europeans.

PATIENTS AND METHODS

Sources of Cases

The study was performed retrospectively from 1 January 1972 to 31 December 1989, inclusive. Potential cases were identified from hospital activity analyses and Korner data, from records held in pathology and endoscopy departments, from registers belonging to general practitioners in Leicestershire and adjoining counties, and personal indexes. People from Leicestershire treated in adjoining districts and at supra-regional referral centres were also identified. Patients treated privately were identified from their general practitioners. Demographic details and the results of laparotomy, histological, microbiological, radiological and endoscopic investigations were noted.

All potential cases were reviewed by Dr Probert and Dr Jayanthi using a structured proforma (Appendix 1) based on Lennard-Jones criteria of case definition [26] (Appendix 2). Inter- and intra-observer variation had been assessed [27].

Case Definition

The diagnostic criteria of Crohn's disease were based on the clinical history and investigations. A history of abdominal pain, with or without diarrhoea, which may be bloody, was necessary. Features sought on investigation were discontinuous disease on endoscopy and/or radiology, with discrete ulcers or strictures. Histological features were transmural inflammation with lymphoid aggregates and goblet cell preservation; non-caseating granulomas were characteristic but not essential for a diagnosis of Crohn's disease. Patients in whom the diagnosis of Crohn's disease was entirely clinical were excluded. Cases of indeterminate colitis, defined as continuous colitis with equivocal histological or endoscopic appearance, were distinguished from Crohn's disease. Patients with secondary colitis were excluded.

Demographic Data

Leicestershire comprises the city of Leicester, population approximately 280,000 of whom 75,000 were South Asian, its adjoining suburbs, several large towns and a large rural area (Fig. 1). Population data were obtained from a variety of published sources [28–33] and also Leicester City Council projections for 1990 (personal communication).

From raw data of 930,000 people registered with the FHSA an age-sex analysis for religious groups was preformed. Ninety-five per cent of the population are registered with a general practitioner [34]. Intermarriage with Europeans is uncommon amongst South Asians [35] and the use of surnames to define religion is reliable [36, 37]. The FHSA data with surname analysis is a useful means of estimating the ethnic mix in the county.

Overall, the ethnic/religious composition of Leicester is better defined than that of the county, so the incidence of Crohn's disease was only calculated for minority groups in the city.



FIG. 1. Leicestershire comprises the City of Leicester, several smaller towns and a large rural area.

Calculations

Data were analysed using Cochran's test [38], a z statistic for populations (39), the χ^2 test, relative risk and 95 per cent confidence intervals [40]. The age-specific incidence was standardized by the direct method [41].

Ethical Committee approval was given for these studies.

RESULTS

Over 2500 potential cases of inflammatory bowel disease were scrutinized, of whom 1420 had ulcerative proctocolitis and 807 Crohn's disease. The remainder had been miscoded as a result of discussions about differential diagnosis in the case notes.

INCIDENCE

Leicester City

One hundred and seventy-nine cases of Crohns disease occurred in the indigenous population of Leicester City and 23 in Asians (Table 1). Europeans had a marginally higher incidence of Crohn's disease than South Asians in the 1970s (z=0.8, ns), the relative risk for Europeans was 2.8 (95 per cent CI 1.1-6.9). From 1981 to 1989 the incidence of Crohn's disease rose in each ethnic group (Table 1): the incidence rose markedly in Muslims whereas in Sikhs and Hindus the rise was smaller. The rise in incidence for Europeans was significant ($\chi^2=8.1$, p<0.005), although not for South Asians ($\chi^2=2.8$, ns) nor in different religious groups; Hindus ($\chi^2=0.9$, ns), Sikhs ($\chi^2=0.3$, ns) and Muslims ($\chi^2=1.6$, ns).

The standardized incidence in Europeans and South Africans was similar in the 1980s, (z=0.8, ns), but the relative risk to Europeans fell to 1.7 (95 per cent CI 1.0-2.9). The risk to Europeans was 2.2 times that of Hindus, but similar to that of Muslims (relative risk 1.0).

TABLE 1. Cases and	incidence	(cases/100,000/year)	of	Crohn's
disease in Leicester				

Year	European	South Asian	Hindu	Sikh	Muslim
1972	7		· ·		
1973	9				
1974	9				
1975	6	1	1		
1976	6				
1977	7	l	1		
1978	13	2	1	1	
1979	12	1			1
1980	6				
Mean standardized Incidence (1972–80)	3.47	1.24	1.4	1.8	0.9
Confidence interval	2.7-4.3	0.1-2.3	0-2.8	0-3.6	0-3.6
1981	14	1			1
1982	8	1			1
1983	15	1		1	
1984	9	4	3		1
1985	12	2 3	1		1
1986	9	3	2 2		1
1987	11	4		2	
1988	13	2	1		1
1989	13				
Mean standardized					
incidence (1981-89)	5.27	3.1	2.4	3.4	5.4
Confidence interval	4.3-6.4	1.7-4.6	0.9-3.2	0-6.7	1.0-8.9

South Asians had significantly less Crohn's disease than Europeans. The incidence has risen in all groups. Hindus are at least risk of Crohn's disease.

County of Leicestershire

Data from the City of Leicester were used together with that from the rest of the county. In the 1970s there were 241 cases amongst Europeans and six amongst South Asians in the County of Leicestershire. The standardized incidence in Europeans in the 1970s was 3.4 cases/ 10^5 /year compared to 1.4 cases/ 10^5 /year in South Asians (z = 1.1, ns). During the 1980s the standardized incidence in the whole county rose to 4.7 cases/ 10^5 /year in Europeans and 3.1 cases/ 10^5 /year in South Asians (Fig. 2). The standardized incidence in South Asians and Europeans were equal from 1986. The increase in incidence was significant in Europeans ($\chi^2 = 12.6$, p < 0.001), but not in South Asians ($\chi^2 = 2.9$, ns). The proportion of South Asian cases born in Africa or South Asia were similar ($\chi^2 = 1.1$, ns).

Sex Ratio and Age-specific Incidence

During the 1970s there was a relative excess of Crohn's disease among European women, (relative risk 1.4, 95 per cent CI 1.1-1.9), however during the 1980s the incidence was equal

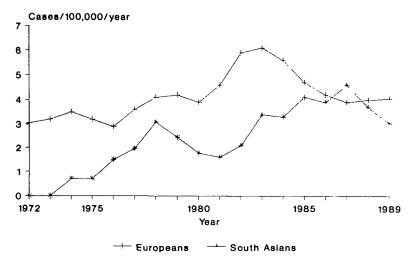


FIG. 2. Standardized incidence of Crohn's disease in the County of Leicestershire. The standardized incidence of Crohn's disease was calculated for each ethnic group for each year for the study. The rolling incidence, shown on the graph, was found using the mean incidence over 3-year periods, for example the value for '1976' was calculated from 1975–77 and '1977' from 1976–78.

(relative risk 1.0, 95 per cent CI 0.8–1.2). The risk to South Asian men was greater than that to women, 17:11.

The incidence was highest in Europeans aged 16-20 years $(9.9/10^5/\text{year})$ and in South Asians aged 31-35 years $(4.9/10^5/\text{year})$. The distribution in Europeans was bimodal, a second peak occurring in people aged 71-75 years (Fig. 3). There was no overall difference in the age-specific incidence values in Europeans ($\chi^2 = 13.4$, ns) and no age band had a significantly increased incidence value. There was no secondary peak in South Asians, however the South Asian population aged over 65 years is only 3000.

Only four of the South Asian patients were born in Britain. Nine others, born after 1960,

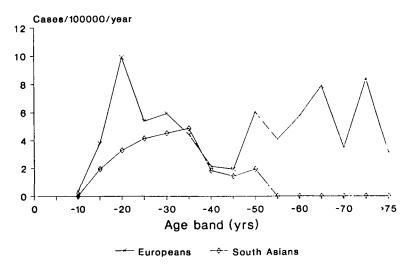


FIG. 3. Age-specific incidence of Crohn's disease in the City of Leicester. The age-specific incidence for South Asians and Europeans is shown for 1972-80 and 1981-89.

were likely to have migrated when young, although the precise age at migration is not known.

Incidence in Children

The incidence in European children increased in the county during the study period: 0.4 cases/10⁵/year in those aged <11 years and 2.2 cases/10⁵/year in those aged 11–15 years in the 1970s, to 0.4 cases/10⁵/year and 3.7 cases/10⁵/year, respectively, during the 1980s. There were no cases in South Asian children under 11 years old, however four cases were diagnosed in children aged 11–15, with an incidence of 0.45 cases/10⁵/year in the 1970s and 2.03 cases/10⁵/year in the 1980s.

Incidence by Disease Site

There was no difference in disease distribution between Europeans and South Asians ($\chi^2 = 3.7$ ns), nor between South Asian ethnic groups ($\chi^2 = 6.2$ ns). In all groups the most common site of disease was the terminal ileum, except in Sikhs where it occurred equally in the colon and terminal ileum (Table 2).

There was a inverse relationship between age and incidence of Crohn's disease of the small bowel in adults, while the incidence of Crohn's disease of the large bowel tended to increase with age. The incidence of colonic Crohn's disease in Europeans rose from 0.7 cases/ 10^5 /year in the 1970s to 1.6 cases/ 10^5 /year in the 1980s. The incidence of disease in other sites remained constant. The proportion of colonic Crohn's disease cases rose significantly ($\chi^2 = 13.6$, p < 0.001) (Fig. 4).

Incidence by Urban-Rural Areas

The city of Leicester and its suburbs and the seven towns were defined as urban and all other areas as rural. The rural incidence during the 1970s was 3.2 cases/10⁵/year and rose to 4.7 cases/10⁵/year in the 1980s (Table 3). There was no statistical difference between the incidence in Leicester and any of the studied towns or between the rural or urban populations at any stage during the study.

				0 1	
	Terminal ileum only	Colonic only	Small and large bowel	Other small bowel only	Perianal/ Proctitis only
Europeans S Asians	77 19	49 5	27 3	11	15
Hindu Sikhs Muslims	12 2 5	1 2 2	3		1

TABLE 2. Disease distribution by ethnic group in Leicester

There was no statistical difference in distribution of Crohn's disease in each ethnic group.

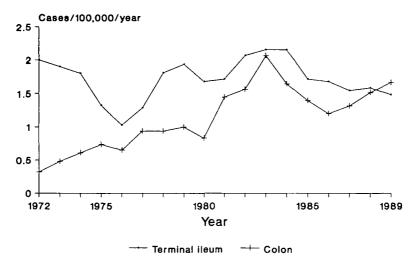


FIG. 4. Incidence of Crohn's disease of different sites. The incidence of CD of the small bowel has remained constant, whilst colonic disease has increased.

FREQUENCY OF COMPLICATIONS

The proportion of Europeans and South Asians undergoing any surgical resection was similar ($\chi^2 = 0.11$, ns). The 330 Europeans and 15 South Asians who underwent surgical treatment for Crohn's disease had a similar number of operations ($\chi^2 = 3.7$, ns). There were 52 panproctocolectomies with ileostomies in the Europeans, and a further four had ileoanal anastomoses. Two South asians underwent colectomy with ileostomy ($\chi^2 = 0.4$, ns).

The complications in Europeans were as follows: fistulae 43, perforations seven, adenocarcinomas six, toxic dilatations two and liver disease one. Two South Asians had fistulae. The complication rates were similar ($\chi^2 = 0.75$, ns).

TABLE 3. Incidence of Crohn's disease in urban and rural areas in Europeans

	1972–80		1981-89	
	Cases	Incidence	Cases	Incidence
Leicester City	74	3.6	105	5.1
Leicester Suburbs	29	3.2	53	5 8
Ashby de la Zouch	1	0.6	2	2.3
Coalville	6	1.1	5	1.9
Hinckley	6	1.2	9	3.6
Loughborough	16	3.6	16	3.6
Market Harborough	9	4.4	6	3.3
Melton Mowbray	7	3.6	13	6.7
Oakham	4	4.4	2	2.3
Rural	87	3.2	128	4.7

There was no statistical difference between the incidence in the City of Leicester and the combination of the seven towns, nor between all urban areas and rural areas.

METHOD OF DIAGNOSIS

There was no difference in the methods used to reach the diagnosis of Crohn's disease (Table 4). All patients studied met similar diagnostic criteria.

DELAY IN DIAGNOSIS

The delay in diagnosis from reported onset of symptoms to proven diagnosis in Europeans (mean 18.2 (SD=44) months) and South Asians (mean 5.7 (SD=11) months) was not significantly different ($\chi^2 = 3.7$, ns).

DISCUSSION

This is the largest detailed study of the incidence of Crohn's disease in South Asians (Table 5). The standardized incidence of Crohn's disease has increased to 3.1 cases/10⁵/year in the 1980s. Although this has occurred in each of the three religious groups the increase was greatest in Muslims. Since 1985 the incidence in South Asians and Europeans in the county has been similar. Thirteen of the 29 South Asian patients were born in Britain or arrived here when they were young: early exposure to an environmental aetiological factor may explain why the incidence in adolescent and young adult South Asians is similar to that of Europeans.

The increase in incidence described in both Europeans and South Asians parallels the change seen in previous reports [1, 3, 7, 8, 10–12, 16, 17]. In Leicester the rise in incidence is largely due to an increase in colonic disease.

The incidence of Crohn's disease in younger children was constant, although it has increased amongst those aged 11–15 years. These results are comparable to those of Barton et al. [18].

Women were at excess risk of Crohn's disease during the 1970s, but this trend disappeared during the 1980s, a finding reported by others [3, 8, 14, 15]. In adults the risk of small bowel Crohn's disease fell significantly with age, but colonic disease was associated with increasing age, a finding noted by others. Such changes in risk may explain the bimodal age distribution in Europeans, which has also been reported in other studies [3, 7, 10, 12–15].

Disease distribution and resection rates were similar in Europeans and South Asians. This finding differs from the situation in ulcerative colitis, where South Asian patients seem to

TABLE 4. Method of diagnosis of Crohn's disease in Leicestershire 1972-89

	Europeans	South Asians
Resected specimen only	114	6
Radiology only	26	2
Endoscopy only	20	1
Histology and radiology	90	4
Histology and endoscopy	75	4
Radiology and endoscopy	44	0
Histology and radiology and endoscopy	189	10
Results from secondary sources only	22	1

There was no difference in the method of diagnosis in the two groups.

TABLE 5. Published data on incidence of Crohn's disease in Europe

Area of study	Duration	No. Cases	Incidence (Cases/10 ⁵ /year)
United Kingdom			
Cardiff (1,2)	1934-87	407	8.3 (1980s)
Derby (3)	1951-85	225	
South Asians		6	4.4 (1980s)
Others		219	7.5 (1980s)
Gloucester (4)	1966–70	19	1.5
Nottingham (5)	1958–72	144	3.6 (1970s)
NE Scotland (6)	1955–68	166	2.2 (1960s)
N. Ireland (7)	1966-81	44 0	1.83
Leicestershire	1972-89	609	
Europeans		581	4.7 (1980s)
South Asians		28	3.1 (1980s)
Denmark			
Copenhagen (8)	1962-78	227	2.7 (1970s)
Faroe Islands (9)	1981-88	66	3.6
Finland (10) Helsınkı	1975-85	193	3.0 (1980s)
Germany (11) Tubingen Co.	1970-84	828	4.0 (1980s)
Iceland (12)	1950-79	33	0.9
Netherlands (13) Leiden	1979-83	210	3.9
N. Norway (14)	1983-86	82	5.8
W. Norway (15)	1984-85	86	5.3
USA			
New York (16)	1973-86	960	3.9 (1980s)
Minnesota (17)	1943-82	103	3.8

have a milder illness than Europeans [27]. There is no evidence of differences between Europeans and South Asians in seeking medical advice for mild Crohn's disease.

There was no evidence of an urban-rural gradient in incidence of Crohn's disease in Leicestershire. Our definition of urban areas was similar to those used in previous studies [42], but earlier reports have shown a higher incidence in urban than rural areas [11, 13, 14, 42]. The lack of difference in this study, as in the study of ulcerative colitis [23], probably reflects commuting habits.

Reports from Asia suggest that Crohn's disease is uncommon. Al-Nakib et al. [20] found the incidence of Crohn's disease in Kuwait to be $0.5/10^5/\text{year}$. A series of 44 cases collected over 10 years by Gupta et al. [19] was exceptional. It is possible that Crohn's disease is confused with abdominal tuberculosis [43–46]: despite the difficulties the conditions can be differentiated with care [47]. A parallel study of abdominal tuberculosis has shown a decline in incidence of this condition [48]. The majority of cases were in South Asians and it is conceivable that Crohn's disease was overlooked because of the frequency of abdominal tuberculosis (Figs. 5, 6). Care must be taken in differentiating these conditions, particularly as the incidence Crohn's disease will soon exceed that of abdominal tuberculosis in South Asians.

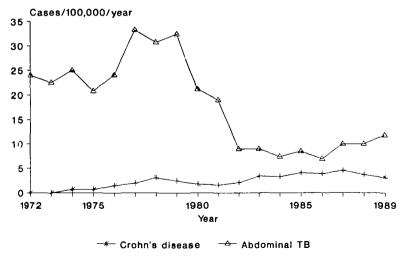


FIG. 5. Incidence of abdominal tuberculosis and Crohn's disease in South Asians. The incidence of abdominal tuberculosis has fallen, but still overshadows that of Crohn's disease.

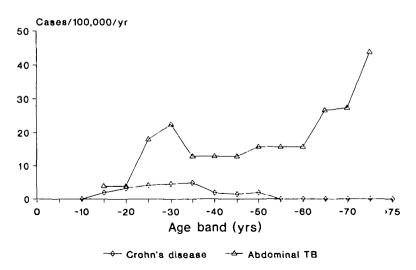


FIG. 6. Age-specific incidence of abdominal tuberculosis and Crohn's disease in South Asians during the 1980s. Crohn's disease affects younger people. Abdominal tuberculosis is more common in adults older than 25 years.

In contrast to ulcerative colitis, smoking is a risk factor for Crohn's disease in Europeans [49] and this may partly explain the similarities between Muslims and Europeans and the lower risk to Hindus, as Muslims are more likely to smoke than Hindus [50].

The cause of Crohn's disease is unknown, but its increasing incidence in people of South Asian descent supports an environmental factor in its aetiology. Further studies of migrants may elucidate the risk factors leading to their different susceptibility and increase our understanding of the aetiology of Crohn's disease.

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