Cystic fibrosis in Asians

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Abstract
The clinical course of cystic fibrosis in nine Pakistani Asians was compared with 18 non-Asian age and sex matched controls. The Asian patients grew *Pseudomonas aeruginosa* at an earlier age (4·0 v 7·5 years), tended to have lower respiratory function test results (forced vital capacity 58·5 v 76·8% predicted; forced expiratory volume in one second 79·8 v 100·3% predicted), and had significantly greater concentrations of immunoglobulin IgG (13·4 v 10·1 g/l). They had a lower weight for age (78·4 v 95·7%) and weight for height (90 v 98·5%) despite similar intakes of dietary energy. Four of the nine Asians carried the ΔF508 mutation compared with 17 of 18 controls. All the Asian patients were born in the UK; seven of their mothers were born in Pakistan and had moderate or severe difficulties with the English language. It is concluded that Asian patients may have a more severe clinical course than matched controls and that genetic and environmental factors may be contributory.

(Arch Dis Child 1993;68:120-2)

Results

DIAGNOSIS

The mode of presentation for the groups was similar. Only one Asian patient presented with meconium ileus. The sibling of another Asian patient died of this complication in the neonatal period. Five controls and two Asian patients were detected by neonatal screening, which has been undertaken at our hospital since 1977. A sweat test was performed on one control patient because his sibling was known to have cystic fibrosis. The remaining patients presented with chest symptoms (3/9 v 2/18) or with gastrointestinal symptoms, including failure to thrive (3/9 v 9/18). When the patients diagnosed by screening were excluded there was no significant difference in the age of onset of symptoms (0·1 v 0·06 years), the age at diagnosis (0·83 v 0·5 years), or the diagnostic delay (0·42 v 0·32 years).

RESPIRATORY DISORDERS

The forced expiratory volume in one second (58·5% predicted v 76·8%) and the forced vital capacity (79·8% predicted v 100·3%) were lower in the Asian patients, but these differences were not significant. Six of the Asian patients and 13 of the controls were able to perform respiratory function tests satisfactorily. Only one Asian patient was receiving either prednisolone by mouth or inhaled budesonide or beclomethasone
treatment for symptoms of bronchial lability compared with five controls.

*Pseudomonas aeruginosa* had been isolated from the sputum of six of the Asian patients and 13 of the controls. This had occurred at a significantly younger age in the Asian subjects (4.0 ± 7.5 years; p < 0.05). None of the Asian patients had grown *Xanthomonas maltophilia* compared with two of the controls, and no patient from either group had grown *Pseudomonas cepacia*. The level of serum immunoglobulin IgG was significantly greater in the Asian patients (134 ± 101 g/l; p = 0.01). An additional diagnosis of hypogammaglobulinaemia has since been made in one of the control patients; her IgG concentration was not included in this comparison. The median Chrisepin-Norman chest radiograph scores were similar for the two groups (5 ± 6). The median Shwachman clinical scores were lower in the Asian patients (80 ± 90; p = 0.07) and respiratory disease was the most important factor accounting for this.

**NUTRITION AND GASTROINTESTINAL**

The weight for age of the Asian patients was significantly less than the controls (78.4 ± 95-7%; p = 0.05), as was the weight for height (87.0 ± 98.8%; p = 0.01). There was no significant difference in height for age (94.7 ± 97.4%). There was also no significant difference between the energy intake at the most recent dietary assessment (111 ± 120-5% of estimated average requirements; p = 0.3). The groups were taking similar numbers of pancreatic enzymes (20 ± 24.5) and there was no significant difference in their facial fat outputs (11.9 ± 13.6 g/day).

**COMPLICATIONS AND GENETICS**

There were surprisingly few complications of cystic fibrosis in the Asian patients (table). One Asian child whose cystic fibrosis presented with meconium ileus was noted to have hepatomegaly in the neonatal period. This has not subsequently resolved. His sibling, born to the same consanguineous parents, does not have cystic fibrosis but has severe and as yet unexplained liver disease.

Two Asian patients had other genetic disorders. One had glucose-6-phosphate dehydrogenase deficiency and the second had distal renal tubular acidosis and β thalassaemia trait. The latter patient has been the subject of a previous report. Four of the nine Asian patients carry the δF508 mutation (all homozygotes) compared with 17 of 18 controls (12 homozygotes).

<table>
<thead>
<tr>
<th>Complication</th>
<th>No of patients with complications at any one time</th>
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</thead>
<tbody>
<tr>
<td>Liver disease</td>
<td>Asians</td>
</tr>
<tr>
<td>Clinical</td>
<td>1</td>
</tr>
<tr>
<td>Biochemical</td>
<td>1</td>
</tr>
<tr>
<td>Distal ileal obstruction syndrome</td>
<td>1</td>
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<tr>
<td>Glucose intolerance or diabetes mellitus</td>
<td>0</td>
</tr>
<tr>
<td>Allergic bronchopulmonary aspergillosis</td>
<td>0</td>
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<tr>
<td>Nasal polyps</td>
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</tr>
<tr>
<td>Rectal prolapse</td>
<td>0</td>
</tr>
<tr>
<td>Pseudo-Barrett's syndrome</td>
<td>0</td>
</tr>
</tbody>
</table>

**SOCIAL AND ENVIRONMENTAL FACTORS**

Four of the nine Asian patients were considered to be poor clinic attenders compared with six of the controls. Three Asians had prolonged periods without regular medical care, two as a result of visits to Pakistan. The chest disease of one and the weight centile of another deteriorated considerably during these periods away from specialist cystic fibrosis care. More of the Asian families were considered to be either moderate or severely non-compliers with treatment (6/9 vs 6/18). There was no difference in the median number of admissions to hospital over a 24 month period for the two groups (three vs one).

The Asian patients were all born in the UK.

Two pairs are cousins. They come from significantly larger families than the non-Asian group (median number of siblings: three vs one; p < 0.05). Their families originate from Pakistan where seven of their mothers and six of their fathers were born. Whereas all the fathers now have no difficulties communicating in English, all their mothers continue to have at least moderate communication difficulties.

All nine Asian families are social class III, IV, or V, compared with 14 of the 18 controls. Five of the parents of the Asian patients are unemployed and the fathers of the other four are employed as an engineer, a butcher, a taxi driver, and a factory worker. None of the Asian families were considered to live in unsatisfactory housing and smoking was significantly less common in the Asian families (1/9 vs 14/18; p < 0.05).

**Discussion**

Cystic fibrosis is the most common potentially lethal genetic disorder in white populations, but it is considerably less prevalent in other ethnic groups. Several reports suggest differences of expression of cystic fibrosis in non-whites and these have been recently documented in North American black subjects. Descriptions of cystic fibrosis in Asians are few, however.

Goodchild et al reported three Asian children from the West Midlands and estimated an incidence of cystic fibrosis in Asians of approximately 1:10 000.1 Schwarz et al found that three of six patients in Lancashire Pakistani families carried the δF508 mutation; all were homozygotes.

Our small study suggests that this group of Asian patients may have a more severe clinical course than matched non-Asian controls. *P aeruginosa* was grown from sputum at a significantly earlier age in the Asian patients and this may adversely affect prognosis. Increased serum IgG concentrations also suggest increased activity of the chest infection, as do the reduced respiratory function tests and Shwachman scores.

As a group the Asian patients were significantly underweight, which has been recognised as an important prognostic factor in cystic fibrosis. This does not appear to be due to more severe intestinal malabsorption or reduced energy intake. Increased energy utilisation as a result of more severe pulmonary disease and genetic factors may have contributed to their lower weight.
Tanner-Whitehouse standards were used in this study in the absence of more specific reference data for UK Asians. In Indian children, however, in the 0–5 year period it has been suggested that socioeconomic and environmental factors determine differences of growth performance rather than genetic factors and therefore Tanner-Whitehouse standards can be used for Indian children.22 23 Nevertheless, this does not indicate that Tanner-Whitehouse standards are necessarily applicable to other ethnic groups.24 Genetic factors may be important in determining differences between the groups. Since the cystic fibrosis mutation was located in 198325 and many studies have sought to correlate clinical phenotype with the genotype of the patient with cystic fibrosis. The most common cystic fibrosis mutation, known as ΔF508, has its highest incidence in northern Europe and the USA.28 A total of 78·5% of cystic fibrosis mutations are accounted for by ΔF508 in native English subjects from north west England.2

Only four of the Asian patients studied carried the ΔF508 mutation; all were homozygous and two were cousins. Five Asians did not carry this mutation. The presence of cystic fibrosis mutations other than ΔF508 may have contributed to the differences of clinical phenotype in the Asian group studied.

The distribution of cystic fibrosis mutations in the Asian population is likely to be strongly influenced by a high incidence of parental consanguinity,29 moreover it increases the probability of other genetic disorders, which were found in two children. This contrasts with the small number of complications of cystic fibrosis observed among the Asian patients. Other genetic diseases in addition to cystic fibrosis should be carefully considered in Asian patients.

Social and environmental factors are also likely to have contributed to the differences observed. All seven of the cases born in Pakistan had moderate or severe communication problems in English. Communication difficulties render education of the Asian family considerably more difficult even when interpreters are available. It may also delay the presentation for treatment during acute respiratory exacerbations of cystic fibrosis, increasing the likelihood of pulmonary damage. No significant delay was noted between the initial onset of symptoms and the clinical diagnosis of cystic fibrosis in the Asian patients, but our study numbers were small and neonatal screening prevented delays in the diagnosis of two Asian patients and four controls. Language difficulties could delay counselling for the prenatal diagnosis of cystic fibrosis and may impede families obtaining state benefits, exacerbating financial hardship.

All of the Asian families were social class III, IV or V, compared with 14 of the 18 controls. This may have been a source of bias in our study.30 None of the Asian families lived in poor housing conditions, however, and the adverse factor of tobacco smoking at their homes was uncommon.31

We conclude that Asian patients may have a more severe clinical course than matched controls and that genetic and environmental factors may be contributory. These families should be given additional help from the cystic fibrosis team to assist in overcoming language and cultural difficulties. A social worker from the same ethnic background as the patient is desirable.

We are grateful to the Cystic Fibrosis Trust for funding Dr Bower and to Drs SP Conway and GM Wilson for permission to study their patients.