Diabetes, hyperinsulinaemia, and coronary risk factors in Bangladeshis in East London

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SUMMARY Immigrants from the Indian subcontinent (South Asians) in England and Wales have higher morbidity and mortality from coronary heart disease than the general population; this seems to apply to both Hindus and Muslims. Studies in north west London and Trinidad found that the increased risk of coronary heart disease in Indians was not explained by dietary fat intakes, smoking, blood pressure, or plasma lipids. In the present study the distribution of coronary risk factors was measured in an East London borough where the mortality and attack rate from coronary heart disease are higher in the Asian population, predominantly Muslims from Bangladesh, than in the rest of the population. In a sample of 253 men and women aged 35-69 from general practice, mean plasma cholesterol concentrations were lower in Bangladeshi than in European men and women. Mean systolic blood pressures were 10 mm Hg lower in Bangladeshis. Plasma fibrinogen concentrations were similar in Bangladeshis and Europeans and factor VII coagulant activity was lower in Bangladeshi than in European men. In contrast with the findings in Hindus in north west London, smoking rates were high in Bangladeshi men and the ratio of polyunsaturated fatty acids to saturated fatty acids in plasma lipids was lower in Bangladeshis than in Europeans. Diabetes was three times more common in Bangladeshis than in Europeans and serum insulin concentrations measured after a glucose load were twice as high in Bangladeshis. High insulin concentrations in Bangladeshis were associated with high plasma triglyceride and low high-density lipoprotein cholesterol concentrations.

Insulin resistance, leading to diabetes, hyperinsulinaemia, and secondary lipoprotein disturbances, is a possible mechanism for the high rates of coronary heart disease in South Asians in Britain and overseas.

Death rates from coronary heart disease in men and women born in the Indian subcontinent (South Asians) who live in England and Wales are higher than in the general population, and this high rate is shared by Gujaratis, Punjabis, South Indians, and Muslims.^{1,2} Similar findings have been reported for other Indian populations overseas.³ In a survey in the north west London boroughs of Brent and Harrow we found that South Asians had lower dietary intakes of saturated fat and cholesterol, higher ratios of dietary polyunsaturated to saturated fat, lower con-

centrations of plasma cholesterol, and smoked less than the average for the British population.⁴ These findings were confirmed in Brent by other investigators⁵ and yet the standardised mortality ratio for coronary heart disease for those born in the Indian subcontinent or East Africa who were resident in Brent or Harrow in 1979-83 was 163 for men and 157 for women.

This study of a Gujarati Hindu population provided no clues to the reasons for the increase in coronary heart disease, and the results did not accord with current thinking on the causes of coronary heart disease. This prompted us to study Muslims from the Sylhet region of Bangladesh who have settled in the East London borough of Tower Hamlets. In 1970-72 Bangladeshi men in this district were first reported to have a higher morbidity from coronary heart dis-

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ease.⁶ The objectives of our study were to determine whether the findings in north west London could be replicated in a Muslim population from the Indian subcontinent and secondly to investigate whether the increases in coronary heart disease in immigrants from the Indian subcontinent in Britain can be explained by other risk factors that were not measured in the earlier study, such as hypertension, increased haemostatic activity, and glucose intolerance.

Methods

SAMPLING

From published reports we estimated the size of difference in the distribution of each risk factor that would give rise to a 20% difference between two populations in coronary heart disease mortality in men. A target sample size sufficient to detect such differences was estimated to be about 80 men in each ethnic group. We obtained approval for the study from local ethics committees.

Fieldwork was undertaken between June 1985 and April 1986. The study area was defined as postal districts E1 and E2—the western half of the borough of Tower Hamlets. Most of the borough's Bangladeshi residents live in this area and are registered with one of three local practices. The lists of these three practices and of a further two practices with mostly native British patients were chosen as the sampling frame. A sample of men born between 1920 and 1949 was chosen from each practice, excluding residents in hostels for the single homeless and those with mental handicap, recent psychiatric illness, terminal malignancy, or other advanced disease. To minimise the proportion of wrong addresses, those who had not consulted their doctor since 1981 or who last attended for immunisation before returning to Bangladesh were also excluded because they were unlikely to be still resident. The proportions sampled from each practice were adjusted to ensure approximately equal numbers of Bangladeshi and control respondents. In three practices which had age-sex registers the sample was stratified by year of birth to give an even distribution across the age range. In the early stages of the study, women aged over 35 years who were married to Bangladeshi respondents were also invited to take part: because of the age difference between husbands and wives this proved to be an unsatisfactory means of sampling older Bangladeshi women. A sample of women was chosen independently from four of the practices in the last four months of fieldwork. In one practice whose list was made up predominantly of Bangladeshi residents, only women born before 1940 were included at this stage. Apart from the exclusions and

the stratification by age, sex, and practice, the sampling procedure was random.

Each eligible person was sent a letter inviting them to participate. We visited addresses from which no reply was received to ascertain whether the address was correct and to issue a further invitation. Of the 557 people to whom letters were sent, 173 had moved to other addresses either outside the district or unknown, two had died, and one was in hospital. Of the 381 remaining, 58 refused, three were medically unfit to take part, and it was not possible to contact 12. Three hundred and eight interviews were completed—a response rate of 81% from those believed to be resident.

Respondents were interviewed at home with a questionnaire including demographic items, smoking, alcohol consumption, and medical history, and invited to attend the London Hospital Medical College for measurement of blood pressure and blood sampling. Most Bangladeshis were interviewed in Bengali (by SR) and most Europeans in English (by DEC or PMM). Those without a history of diabetes were asked to fast overnight and consume a 75 g glucose drink an hour and a half before their appointment. Two hundred and fifty three participants attended for examination, giving a final response rate of 66%. The target sample size was reached for men but not for women. Table 1 shows the age distribution of the respondents. There were few Bangladeshi women who were younger than 45 or older than 54. This was a result of the unusual demographic structure of the population and the restriction of the Bangladeshi sample to women born before 1940 in the later stages of the fieldwork. Blood pressure was measured twice with a random zero sphygmomanometer after the subject had been sitting quietly for five minutes: all measurements were made by one observer (PMM). A single venous sample was obtained from 247 of the 253 attenders: in those who had been given a glucose load this was taken as close as possible to two hours after the reported time of consumption.

LABORATORY ANALYSES

Plasma treated with edetic acid was kept at 4°C for up to 48 hours before analysis. High density lipoprotein

Table 1 Numbers attending field station by age, sex, and ethnic category

Age (yr)	Men		Women	
	Bangladeshi	Non-Asian	Bangladeshi	Non-Asian
35-44	17	22	3	12
45-54	35	35	38	11
55-64	22	31	4	18
65-69	2	2		1
All	76	90	45	42

was separated by precipitation with heparin-manganese chloride; cholesterol in these specimens and in whole plasma was measured enzymatically in a centrifugal analyser. The concentration of plasma glucose was measured on a fluoride oxalate specimen by the glucose oxidase method. Fibrinogen concentrations in fresh citrated plasma were measured by a gravimetric method.⁷ Citrated plasma samples for factor VII determination were stored in liquid nitrogen, thawed at 37°C, and maintained at room temperature to avoid cold activation. We assayed factor VII coagulant activity by a manual method based on that of Brozovic *et al*⁸ with immuno AG 100% reference plasma in doubling dilutions from 1/10 to 1/360, 0.025 mol/l calcium chloride, and 1 in 32 rabbit brain thromboplastin. Factor VII deficient plasma was prepared from oxalated bovine blood by a modification⁹ of the method of Lechner and Deutsch.⁹ We measured the fatty acid composition of plasma lipids of a random subsample of those seen in the last six months of fieldwork by a technique described previously.⁴ Insulin concentrations in stored serum were measured by a double antibody technique.¹⁰

STATISTICAL ANALYSES

Mortality ratios for particular boroughs, expressed as percentages and determined for each sex separately, are based on population figures from the 1981 Census and on death records supplied by the Office of Population Censuses and Surveys. The standardised mortality ratio compares the observed number of deaths from coronary heart disease in Bangladeshis with the number that would be expected if the age specific mortality rates were the same in Bangladeshis as in all residents of the borough. The proportional mortality ratio compares the observed number of deaths from coronary heart disease in Bangladeshis with the number that would be expected if, in each age group, the proportion of deaths attributed to coronary heart disease were the same in Bangladeshis as in the general population of the borough. Unlike the standardised mortality ratio, the proportional mortality ratio does not depend on Census data and it measures the extent to which excess coronary mortality is cause specific.

All those of South Asian origin were included in the group referred to as Bangladeshi and all other subjects, including three Afro-Caribbeans, have been assigned to the non-Asian group: this is consistent with the grouping used in analyses of local morbidity and mortality. Participants were classified as diabetic if diabetes had been diagnosed or if their post-load plasma glucose was ≥ 11 mmol/l. Known diabetic patients were excluded from the data for plasma insulin and triglycerides because they did not

fast or receive a glucose load. To test for differences between ethnic groups we analysed data separately for men and women using a least squares linear model. Age was treated as a categoric variable with three levels corresponding to the age groups 35–44, 45–54, and 55–69 years. Adjusted means are the values predicted in the model when all covariates are held at their mean values. Other covariates—body mass index, triglycerides, and insulin—were treated as continuous variables. Triglyceride and insulin values were log transformed for these analyses but have been transformed back to SI units for the tabulations. In figs 1 and 2 data for women are given for only two age bands because of small numbers of Bangladeshi women at the extremes of the age range.

Results

QUESTIONNAIRES

Eighty nine per cent of Bangladeshi men and 80% of non-Asian men belonged to social classes III manual or IV by the Registrar General's classification.¹¹ Fifty three per cent of Bangladeshi men and 20% of non-Asian men were unemployed. Ninety seven per cent of Bangladeshis were Muslim and 91% were from Sylhet. Although most Bangladeshi men were

Fig 1 Concentrations of plasma total cholesterol and high density lipoprotein cholesterol by age, sex, and ethnic category.

Fig 2 Concentrations of plasma triglycerides and serum insulin by age, sex, and ethnic category.

cigarette smokers, only 23% smoked > 15 cigarettes daily compared with 34% of non-Asian men. Ninety three per cent of Bangladeshi men and all Bangladeshi women were abstainers from alcohol.

CLINICAL AND LABORATORY FINDINGS (TABLES 2 AND 3)

Average systolic blood pressures were 10 mm Hg lower in Bangladeshis than in non-Asians and about half of this difference disappeared after adjustment for body mass index. Concentrations of high density

lipoprotein cholesterol were much lower and those of triglycerides much higher in Bangladeshis. The relation between age and systolic blood pressure, plasma cholesterol, plasma triglycerides, and serum insulin was less pronounced in Bangladeshis than in non-Asians (figs 1 and 2). The proportions of essential fatty acids of the $\omega 6$ series (predominantly linoleic acid) in plasma lipids and the polyunsaturated/saturated ratio were lower in Bangladeshis than in non-Asians (table 3). Concentrations of fatty acids of the $\omega 3$ series were slightly higher in the Bangladeshis: this is consistent with their high consumption of fish. Values for factor VII coagulant activity correlated with plasma cholesterol, but only part of the difference in factor VII activity between Bangladeshi and non-Asian men was explained by the difference in plasma cholesterol.

More than 20% of Bangladeshi men and women had diabetes. This was three times the rate in non-Asians (table 4). Two thirds of those with diabetes were already diagnosed: this proportion was similar in both groups. Serum concentrations of insulin after a glucose load were about twice as high in Bangladeshis as in non-Asians (fig 2). This difference persisted after controlling for the time of sampling. The insulin/glucose ratio was also higher in Bangladeshis. Insulin concentrations correlated with body mass index within each group. Insulin and triglyceride concentrations correlated with each other and inversely correlated with high density lipoprotein cholesterol: some of the difference in the concentrations of high density lipoprotein cholesterol between Bangladeshis and non-Asians was accounted for by the differences in plasma insulin and triglycerides.

Discussion

Although the surname analysis of deaths of Asians nationally² and the 1970-72 register⁶ suggest that the high rates for coronary heart disease in immigrants from the Indian subcontinent in Britain are shared by the Bangladeshi population of Tower Hamlets, it is difficult to confirm this by analysis of local mortality data because the numbers of deaths are small. During 1979-83 there were 49 deaths from coronary heart disease among men born in Bangladesh aged 20-69 who were resident in Tower Hamlets; the standardised mortality ratio for coronary heart disease in Bangladeshi men was 118 (95% confidence interval 85-151) and the proportional mortality ratio was 132 (95% confidence interval 105-176). These estimates are consistent with the national data for coronary heart disease mortality in immigrants from the Indian subcontinent (South Asians). Bangladeshi women in Tower Hamlets are not yet old enough for

Table 2 Risk factors (mean (SE), age adjusted for all variables except height) for coronary heart disease by sex and ethnic category

Risk factor	Men		Women	
	Bangladeshi	Non-Asian	Bangladeshi	Non-Asian
Current smokers (%)	82	45	22	39
Height (cm)	165 (1)	171 (1)	151 (1)	160 (1)
Body mass index (kg/m ²)	23.9 (0.4)	26.6 (0.4)	23.7 (1.0)	26.1 (0.7)
Systolic blood pressure (mm Hg)	119 (2)	129 (2)	113 (3)	123 (3)
Diastolic blood pressure (mm Hg)	78 (1)	81 (1)	75 (3)	78 (2)
Plasma fibrinogen (g/l)	3.03 (0.11)	3.14 (0.10)	3.04 (0.12)	3.17 (0.09)
Plasma factor VIIc (% of reference value)	90 (4)	105 (3)	97 (7)	99 (1)
Plasma total cholesterol (mmol/l)	5.53 (0.15)	6.02 (0.13)	5.37 (0.25)	6.09 (0.18)
Plasma HDL cholesterol (mmol/l)	1.13 (0.04)	1.43 (0.04)	1.19 (0.08)	1.45 (0.05)
Percentage of total cholesterol as HDL	21.3 (1.0)	25.3 (0.9)	22.4 (1.5)	25.2 (1.0)
Plasma triglycerides (mmol/l)	2.59 (0.22)	1.76 (0.13)	1.77 (0.26)	1.10 (0.11)
Serum insulin (mU/l)	65 (8)	32 (4)	57 (13)	27 (4)

HDL, high density lipoprotein.

deaths from coronary heart disease to be common in this group (two deaths observed during 1979–83, 1.8 expected).

This study confirms that the excess of coronary heart disease among South Asians in Britain is not explained by raised concentrations of plasma cholesterol. Though no direct dietary measurements were made in this study, the low plasma cholesterol and low polyunsaturated/saturated ratio in plasma lipids are consistent with lower intakes of total fat in Bangladeshis than non-Asians, if the Keys equation¹² (a standard formula for predicting plasma cholesterol from dietary fat intake) holds. It is unlikely that the high dietary total fat intake and polyunsaturated/saturated ratio reported in a study of 12 Bangladeshi men in this district are representative of the average

diet of this population.¹³ The relatively high plasma cholesterol of Bangladeshi men aged under 45 years suggests that this group may be following a less traditional diet. The high proportion of smokers among Bangladeshi men differs from the low smoking rates of South Asian men recorded in north west London⁴ and in a nationally representative sample.¹⁴ The low concentrations of polyunsaturated fatty acids of the $\omega 6$ series in Bangladeshis contrast with the very high concentrations in Hindus in north west London. Although smoking and a low ratio of dietary polyunsaturated/saturated fat may contribute to the high rate for coronary heart disease of Bangladeshi men in East London, they cannot explain the national mortality pattern.

The high prevalence of diabetes, the hyperinsulin-

Table 3 Fatty acid composition of cholesterol esters by sex and ethnic category (mean (SE))

	Men		Women	
	Bangladeshi (27)	Non-Asian (44)	Bangladeshi (37)	Non-Asian (38)
Saturated (%)	14.2 (0.3)	12.8 (0.2)	14.2 (0.2)	12.3 (0.2)
	$p < 0.001$		$p < 0.001$	
Polyunsaturated: $\omega 6$ series (%)	56.6 (1.4)	58.3 (1.1)	55.3 (0.9)	60.1 (0.9)
	NS		$p < 0.01$	
$\omega 3$ series (%)	2.78 (0.22)	2.23 (0.17)	3.38 (0.16)	2.72 (0.16)
	$p = 0.05$		$p < 0.01$	
Ratio of polyunsaturated to saturated	4.28 (0.18)	4.81 (0.14)	4.21 (0.14)	5.21 (0.14)
	$p < 0.05$		$p < 0.001$	

Table 4 Frequency of diabetes by age, sex, and ethnic category

Age (yr)	Men		Women	
	Bangladeshi	Non-Asian	Bangladeshi	Non-Asian
35-44	2/17	1/22	1/2	0/12
45-54	10/32	4/34	9/36	0/11
55-64	4/22	3/28	0/3	3/18
All, age-adjusted	22%	10%	23%	4%

Odds ratio Bangladeshi : non-Asian = 3.1 ($p < 0.01$).

aemia after a glucose load, the high concentrations of plasma triglycerides, and low concentrations of high density lipoprotein cholesterol found in this South Asian population are all factors associated with increased risk of coronary heart disease in other populations: they appear to be part of a general pattern found in South Asians overseas and may represent different manifestations of a single metabolic disturbance. The 22% prevalence of diabetes in this small sample is similar to the figure reported for other populations of South Asians overseas¹⁵⁻¹⁷ but much higher than the 1.3% in a comparable survey in East Pakistan in 1964.¹⁸ Plasma concentrations of insulin have been reported to be higher in Asians than Europeans in South Africa^{19,20} and in a hospital-based sample in West London.²¹ High concentrations of triglycerides and low concentrations of high density lipoprotein cholesterol in South Asians compared with Europeans have also been reported in Trinidad²² and the United States.^{23,24} In our small sample there was no sex difference in the concentrations of high density lipoprotein cholesterol in either the Bangladeshi or the other groups: while absence of sex difference has been reported in other South Asian populations^{4,25,26} the absence of the usual sex difference of about 0.3 mmol/l in the European group is puzzling since the 95% confidence interval for the difference (-0.15 to $+0.15$ mmol/l) is less than the usual difference and it is therefore unlikely to be explained entirely by chance or random measurement error.

Associations between raised concentrations of plasma insulin, high concentrations of triglycerides, and low concentrations of high density lipoprotein cholesterol have been reported in other populations²⁷⁻²⁹: hyperinsulinaemia increases the synthesis of very low density lipoprotein triglyceride synthesis^{27,30} and this may have a reciprocal effect on the concentration of high density lipoprotein cholesterol.³¹ Definitive demonstration of insulin resistance requires steady state measurements of glucose disposal and insulin concentrations, but the parallel findings of a raised insulin/glucose ratio and high frequency of diabetes in this South Asian population make it reasonable to infer that insulin resistance

underlies the increased insulin concentrations.

The high insulin concentrations in Bangladeshis were not explained by high body mass index; however, this index may be inappropriate for comparing adiposity in groups with different mean frame sizes.³² In other populations insulin concentrations are more closely related to deposition of fat on the upper body, which was not measured in this study, than to body mass index.³³ Pathological and epidemiological evidence support the view that the combination of raised plasma insulin, raised triglycerides, and low concentrations of high density lipoprotein cholesterol is atherogenic.³⁴⁻³⁶

Our results and those of other investigators indicate that the evidence relating to high fat diet, plasma cholesterol, hypertension, and smoking to the occurrence of coronary heart disease does not account for the high rates of coronary heart disease rates in South Asians overseas¹⁵; any attempt at an explanation must therefore invoke less well established risk factors. On the basis of these findings we suggest a unitary hypothesis for the mechanism of high rates of coronary heart disease and diabetes in South Asians overseas: insulin resistance may be responsible for hyperinsulinaemia, secondary disturbances of lipoprotein metabolism, and a high prevalence of non-insulin-dependent diabetes. This metabolic pattern might lead to accelerated atherogenesis either through a direct effect of insulin upon the arterial wall or as a result of the changes in lipoprotein concentrations. We are now planning a larger study to test this hypothesis and to investigate the relation of these metabolic differences to adiposity, diet, physical activity, and social environment. If the hypothesis is correct then measures to reduce hyperinsulinaemia, such as weight reduction and increased exercise, may be the most effective means of preventing coronary heart disease in South Asians.

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