Lipid and Carbohydrate Metabolic Risk Markers for Coronary Heart Disease and Blood Pressure in Healthy Non-obese Premenopausal Women of Different Racial Origins in the United Kingdom

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Metabolic risk markers for coronary heart disease (CHD) were determined in apparently healthy females of differing racial origins residing in the United Kingdom. The females were of black (n = 122), Oriental (n = 114), South Asian (n = 128), and white (n = 271) origin, premenopausal, non-obese, and aged 16 to 45 years. In comparison to whites, South Asians had lower serum high-density lipoprotein (HDL) cholesterol and HDL_2 cholesterol and higher fasting and oral glucose tolerance test plasma insulin responses. Black females had higher fasting plasma and oral glucose tolerance test insulin and lower serum triglyceride and glucose compared with white females. Orientals differed from whites in having higher fasting and oral glucose tolerance test insulin concentrations. Resting systolic or diastolic blood pressures, total serum cholesterol, HDL_3 cholesterol, and low-density lipoprotein (LDL) cholesterol did not differ between groups. Whereas previous studies have demonstrated similar differences in representative samples from different ethnic communities, our results clearly demonstrate that differences also exist in young healthy females, individuals considered to have the least risk of CHD.

THERE ARE considerable geographic differences in coronary heart disease (CHD) mortality. The World Health Organization MONICA project reported an eight-fold ratio between the highest and lowest age-standardized ischemic heart disease mortality for men and a 13-fold ratio for women both aged 35 to 64 years.[1] It has been hypothesized that this variation results from differences in lifestyle, environment, levels of risk markers and their effects, socioeconomic status (SES), and ethnic origin.[1-3] The influence of the environment may be particularly important, since immigrants from populations with a low incidence of heart disease have been shown to assume a CHD incidence intermediate between their original and host country rates.[4] However, an excess of CHD mortality has been observed in immigrants of South Asian origin relative to indigenous populations in several parts of the world.[5] This excess is also observed in England and Wales, where members of both genders display an increased standardized mortality ratio of approximately 40% relative to the general population.[6] In contrast, men and women of Caribbean origin display lower standardized mortality ratios for CHD (45% and 76%) than the population of England and Wales.[6] Besides examining the factors of smoking habit, hemostasis, diet, and prevalence of non–insulin-dependent diabetes mellitus, previous studies of immigrants of South Asian[7-9] and Caribbean descent[9,10] residing in the United Kingdom have documented differences in metabolic risk factors for CHD that may partly explain these differences. To extend the results to the general population, these studies have generally used broad inclusion criteria with regard to age and obesity. To what extent these reported differences are present in healthy young individuals is not established. In the present study, we have assigned healthy non-obese premenopausal females residing in the United Kingdom to one of four different racial groups, and measured CHD risk markers relating to lipid and carbohydrate metabolism and blood pressure. We have compared the levels of risk markers in young female immigrants and young white females born and residing in the United Kingdom.

SUBJECTS AND METHODS

Subjects

Six hundred thirty-five females were studied. All subjects, regardless of group, were self-referred volunteers contacted through inner-city family planning clinics, general practitioner practices, or personal contact. For inclusion in the study, subjects were required to be within 20% of ideal body weight (Documenta Geigy), aged 16 to 45 years, premenopausal, and in apparently good health, and not to be receiving treatment for any previous disease. In addition, they were not taking any drugs (including oral contraceptives) likely to affect carbohydrate or lipid metabolism. Occult hepatic and renal disease were excluded by routine biochemical tests performed on samples obtained when metabolic tests were undertaken. Women found to have a fasting venous plasma glucose above 7.8 mmol/L or a venous plasma glucose greater than 11.1 mmol/L 2 hours after an oral glucose tolerance test were excluded from the study. The protocol was approved by the ethics committee of St Mary's Hospital, London, and informed consent was obtained from each patient.

Subjects were assigned to one of four racial groups, namely black (n = 122), Oriental (n = 114), South Asian (n = 128), and white (n = 271). Assignment to a group was performed on the basis of appearance, self-assignment by the volunteer, and grandparental country of origin with at least three of four grandparents belonging to the same group. Except for the white group, all participants were immigrants to the United Kingdom with a minimum duration of residence of 1 year. Subjects of black descent were immigrants from Caribbean (67%) and African (33%) countries. Major countries of origin for the 114 Oriental females were Malaysia (40%), the Philippines (24%), China (9%), and Japan (6%). Subjects of South Asian descent had immigrated from India and Sri-Lanka (33%), Africa (47%), the Caribbean (9%), and Pakistan and Bangladesh (4%). The white group were United Kingdom born and resident individuals of caucasion descent.

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Day Ward Protocol

Subjects visited the metabolic day ward between days 21 and 27 of their menstrual cycle. Before visiting the day ward for an oral glucose tolerance test, patients were instructed to consume a carbohydrate-rich diet (> 200 g/d) for 3 days to lessen the effects of any dietary variation on insulin secretion, to fast overnight, and to avoid smoking on the morning of the visit. A medical history was obtained. Age, weight, and height were recorded, and a questionnaire assessing racial origin was completed. Subsequent to the study's commencing, it was decided that information relating to smoking habit be recorded. Consequently, tobacco smoking, expressed as current daily tobacco consumption, was recorded in a subset of 417 subjects: 142 whites, 87 blacks, 88 Orientals, and 100 South Asians. After insertion of an indwelling cannula into an antecubital vein, subjects rested semirecumbent for 30 minutes to standardize the effect of posture on lipid and lipoproteins[11] and to provide for measurement of resting blood pressure. Blood pressure was measured by a cuff method, with first- and fourth-phase Korotkoff sounds being recorded. Fasting serum samples were taken for determination of total cholesterol, triglyceride, and lipoprotein cholesterol. Two samples taken 10 minutes apart were collected into lithium-heparin tubes on ice and used for determination of fasting plasma glucose and insulin. The patients then drank a glucose solution (1.0 g glucose/kg body weight as a solution of 50% wt/vol D-glucose). Further heparinized samples were collected every 30 minutes for the next 3 hours. Heparinized blood tubes were kept on ice and centrifuged within 30 minutes. Plasma was divided into aliquots and either assayed for glucose or stored at −20°C for subsequent insulin assay. Serum samples were stored at room temperature for 1 hour before low-speed centrifugation and serum separation.

Laboratory Methods

Serum total cholesterol and triglyceride were assayed by semiautomated fluorometric methods.[12,13] Plasma glucose was assayed by a glucose oxidase method.[14] Plasma insulin immunoreactivity was determined by radioimmunoassay using a polyclonal antiserum.[15] In addition, lipoprotein measurements instituted during the course of this study were undertaken on subgroups of subjects: high-density lipoprotein (HDL) cholesterol in 257 and HDL subfractions in 165. HDL cholesterol level was measured after sequential precipitation with heparin and manganese ions,[16] and HDL_3 cholesterol was assayed after precipitation with dextran sulfate.[17] Between-assay coefficients of variation were 2.9% (glucose), 6.1% (insulin), 2.3% (total cholesterol), 3.5% (HDL cholesterol), 8.0% (HDL_3 cholesterol), and 3.0% (triglyceride).

Data Analyses

Serum HDL_2 cholesterol was calculated as HDL cholesterol minus HDL_3 cholesterol. Serum low-density lipoprotein (LDL) cholesterol was calculated using the Friedewald equation.[18] Fasting plasma glucose and insulin levels were calculated as the mean of two samples taken before administration of oral glucose. Total glucose and insulin areas were calculated using the trapezoidal rule, and incremental glucose and insulin areas above the fasting level were calculated.[19] Body mass index (BMI) was calculated as weight divided by height squared.

Triglyceride, fasting insulin, and incremental insulin area values were logarithmically transformed to normalize their distributions. Group differences in age, BMI, metabolic measures, and blood pressure were examined by one-way ANOVA. Where significant variance was found, differences between each immigrant group and the white group were evaluated by unpaired *t* test with Bonferroni correction for multiple comparisons. Differences in the proportion of cigarette smokers between white and immigrant groups were evaluated by χ^2 test.

Metabolic measures and blood pressures were standardized to account for intergroup differences in age, BMI, and parity. Standardization was to the mean value for the entire study group. Significant intergroup differences in regression slopes were observed upon initial analysis. Consequently, standardization was undertaken in each of four groups separately using regression coefficients derived for each group. Group differences in standardized data were examined as described earlier for unstandardized data.

An additional multiple linear regression analysis was undertaken on the subset of subjects for whom smoking data were available to allow for the possible confounding of intergroup differences by smoking. This used age, BMI, parity, and current tobacco consumption as independent variables.

A further multiple linear regression analysis for black, Oriental, and South Asian groups was undertaken using years of United Kingdom residence in addition to the independent variables of age and BMI. All analyses were performed using BMDP 1990 PC-EM statistical software.

RESULTS

Patients

Patient characteristics for the groups are shown in Table 1. Blacks, Orientals, and South Asians were older than whites. Blacks had a significantly higher mean BMI and Orientals had a significantly lower BMI as compared with whites. Mean parity was similar in Oriental females but

Table 1. Age, BMI, Parity, Percentage Current Smokers, and Years of UK Residence in 635 Females of Different Racial Origin

Variable	White (n = 271)	Black (n = 122)	Oriental (n = 114)	South Asian (n = 128)	*P* (ANOVA)
Age (yr)	24.6 ± 6.1	28.1 ± 7.2	28.0 ± 5.3	28.4 ± 7.4	<.0001
*P**	—	<.001	<.001	<.001	
BMI (kg/m²)	21.7 ± 2.1	22.7 ± 2.4	20.5 ± 1.8	21.4 ± 2.2	<.0001
*P**	—	<.001	<.001	NS	
Parity	0.41 ± 1.0	1.4 ± 2.0	0.39 ± 1.1	0.77 ± 1.3	<.0001
*P**	—	<.001	NS	<.05	
Percentage current smokers	28	28	9.1	11	—
P†	—	NS	<.001	<.001	
Years of UK residence postimmigration	—	11.5 ± 6.1	5.2 ± 3.4	8.2 ± 5.6	<.0001

NOTE. Except for percentage current smokers, values are the mean ± SD.

*Versus white group, unpaired *t* test with Bonferroni correction.

†Versus white group, χ^2 test.

higher in black and South Asian females in comparison to whites. The percentage of subjects currently smoking varied across racial groups. Both white and black groups contained a similar prevalence of subjects currently smoking, while Oriental and South Asian groups exhibited a lower prevalence of smoking in comparison to whites. The three immigrant groups exhibited differences in years of residence in the United Kingdom, with blacks having resided the longest.

Glucose and Insulin

Table 2 shows fasting levels and oral glucose tolerance test incremental areas for glucose and insulin standardized for age, BMI, and parity. Blacks, Orientals, and South Asians had significantly higher fasting insulin than whites, but blacks alone had significantly lower fasting glucose. Similarly, blacks, Orientals, and South Asians had higher incremental insulin areas. Intergroup differences in unstandardized data were again generally similar to those seen after standardization (results not shown). Exceptions to this included unstandardized Oriental group mean values for fasting insulin (43.7 pmol/L) and incremental insulin area (26.7 nmol/L · min), which did not differ significantly from the white group means (41.0 pmol/L and 24.9 nmol/L · min).

Lipids

Total cholesterol, triglyceride, and lipoprotein cholesterol levels standardized for age, BMI, and parity are also shown in Table 2. No significant differences were seen between the groups in total cholesterol, LDL, or HDL_3 cholesterol. Blacks had significantly lower triglyceride levels than whites. South Asians had significantly lower HDL and HDL_2 cholesterol as compared with whites. Differences between groups in unstandardized data were generally similar to those that were apparent after standardization (results not shown), except for HDL_2 cholesterol in South Asians, which was nonsignificantly lower than in whites (0.55 *v* 0.65 mmol/L).

Blood Pressure

Resting systolic and diastolic blood pressures after standardization for age, BMI, and parity are shown in Table 2. No significant differences were observed. Similar nonsignificant intergroup differences were seen when unstandardized data were examined (results not shown).

Current Tobacco Consumption

Current tobacco consumption was not repeatedly associated with metabolic variables or blood pressure across

Table 2. Glucose, Insulin, Lipids, Lipoproteins, and Resting Blood Pressure in 635 Females of Different Racial Origin

	White (n = 271)	Black (n = 122)	Oriental (n = 114)	South Asian (n = 128)	*P* (ANOVA)
GLUC (mmol/L)	4.67 ± 0.45	4.45 ± 0.41	4.77 ± 0.41	4.63 ± 0.46	<.0001
*P**	—	<.001	NS	NS	
GLUC IAREA (mmol/L · min)	206.1 ± 138	184.4 ± 111	217.8 ± 149	183.9 ± 152	NS
*P**	—	—	—	—	
INS (pmol/L)†	39.2 (−20.2, +41.6)	50.7 (−29.3, +69.6)	52.3 (−21.1, +35.3)	54.3 (−22.9, +39.6)	<.0001
*P**	—	<.01	<.001	<.001	
INS IAREA (nmol/L · min)†	23.7 (−9.45, +18.4)	28.8 (−12.3, +21.6)	34.4 (−12.0, +18.4)	34.6 (−12.8, +20.2)	<.0001
*P**	–	<.01	<.001	<.001	
CHOL (mmol/L)	4.48 ± 0.78	4.36 ± 0.87	4.41 ± 0.67	4.32 ± 0.78	NS
*P**	—	—	—	—	
TRIG (mmol/L)†	0.73 (−0.22, +0.31)	0.59 (−0.18, +0.26)	0.77 (−0.21, +0.29)	0.72 (−0.23, +0.34)	<.0001
*P**	—	<.001	NS	NS	
	(n = 80)	(n = 56)	(n = 50)	(n = 71)	
HDL-CHOL (mmol/L)	1.57 ± 0.33	1.51 ± 0.31	1.47 ± 0.31	1.36 ± 0.27	<.001
*P**	—	NS	NS	<.001	
LDL-CHOL (mmol/L)	2.66 ± 0.70	2.62 ± 0.86	2.54 ± 0.54	2.55 ± 0.57	NS
*P**	—	—	—	—	
	(n = 50)	(n = 33)	(n = 31)	(n = 51)	
HDL_2-CHOL (mmol/L)	0.68 ± 0.31	0.68 ± 0.28	0.54 ± 0.30	0.54 ± 0.23	<.05
*P**	—	NS	NS	<.05	
HDL_3-CHOL (mmol/L)	0.94 ± 0.21	0.84 ± 0.23	0.90 ± 0.18	0.85 ± 0.21	NS
*P**	—	—	—	—	
	(n = 271)	(n = 122)	(n = 114)	(n = 128)	
SRBP (mm Hg)	108 ± 11.8	107 ± 12.9	106 ± 9.9	108 ± 10.7	NS
*P**	—	—	—	—	
DRBP (mm Hg)	68.9 ± 9.1	68.7 ± 11.8	68.1 ± 8.0	67.7 ± 8.7	NS
*P**	—	—	—	—	

NOTE. Values are the mean ± SD adjusted for age, BMI, and parity; asymmetric SD values were obtained by back-transformation.

Abbreviations: GLUC, fasting glucose; INS, fasting insulin; GLUC IAREA, incremental glucose area; INS IAREA, incremental insulin area; CHOL, total cholesterol; TRIG, triglyceride.

*Versus white group, unpaired *t* test with Bonferroni correction performed if ANOVA *P* (F) < .05.

†Values derived from logarithmic-transformed data.

racial groups after multiple linear regression analysis with age, BMI, parity, and current tobacco consumption as independent variables. Current tobacco consumption was weakly inversely associated with incremental insulin area ($\beta = -0.069$, SE = 0.033, $P = .04$) and inversely associated with HDL cholesterol ($\beta = -0.054$, SE = 0.024, $P = .03$) in black females. Current tobacco consumption was associated with HDL cholesterol ($\beta = 0.086$, SE = 0.037, $P = .03$) and inversely with LDL cholesterol ($\beta = -0.15$, SE = 0.066, $P = .03$) in Oriental subjects.

Years of UK Residence

Years of UK residence was only infrequently associated with metabolic measures in black, Oriental, or South Asian groups using multiple regression analysis with age, BMI, and years of UK residence as independent variables. Positive associations between years of UK residence and HDL_2 cholesterol ($\beta = 0.018$, SE = 0.0084, $P = .04$) were seen only in the black group, and with total cholesterol ($\beta = 0.030$, SE = 0.012, $P = .02$) in South Asians. A weak negative association between years of UK residence and HDL_3 cholesterol ($\beta = -0.014$, SE = 0.0068, $P = .05$) was seen only in the black group. No significant associations were seen between years of UK residence and systolic or diastolic blood pressures in black, Oriental, or South Asian groups.

DISCUSSION

Premenopausal females of various racial origins differed from UK-resident white females in levels of metabolic risk markers for CHD. These differences were not uniform across the three immigrant groups studied and, with few exceptions, were seen in both unstandardized and standardized data. Recently, an association of CHD risk factors in individuals has been documented: the insulin resistance syndrome.[20,21] Insulin resistance and its attendant hyperinsulinemia are hypothesized to be associated with hypertension, hypertriglyceridemia, decreased HDL cholesterol, and impaired glucose tolerance.[20] However, racial differences have been described in the relationship between hyperinsulinemia, insulin resistance, and hypertension,[22] so there may be interracial differences in relationships between other components of the insulin resistance syndrome.

Females of South Asian origin displayed metabolic differences as compared with white females, which were characterized by lower serum total HDL cholesterol and HDL_2 cholesterol and by hyperinsulinemia in both the fasted state and after a glucose challenge. These changes accord with a previous suggestion that the insulin resistance syndrome may be responsible for CHD mortality in South Asians overseas.[7] Lower total cholesterol and HDL cholesterol and hyperinsulinemia have been reported in South Asian females resident in UK communities.[7,23,24] The lower HDL cholesterol could not be explained by tobacco smoking in the South Asian group in our study. In prospective studies, HDL cholesterol level has been inversely associated with development of CHD in white males,[25] females,[26] and males of Indian and African origin.[27] Although HDL subclasses were not assayed in these studies, decreases in HDL cholesterol are not consistently associated with decreases in a particular subclass of HDL cholesterol in South Asians. Men of Indian descent resident in London exhibited lower HDL_2 rather than HDL_3 cholesterol.[9] However, the converse was seen in Indian males in a Trinidad community.[28] Also, Bradford-resident Asian men exhibited lower HDL_2 and HDL_3 cholesterol as compared with non-Asian males.[29] The HDL_2 subclass has been found to be more closely associated with coronary atherosclerosis than HDL_3 in most studies of white subjects.[30] Hyperinsulinemia has been similarly shown to be associated with the occurrence of CHD in white males.[31] In contrast, an elevated blood triglyceride level observed in males and females of UK South Asian communities[7,23] and in South Asians residing overseas[5] was not seen in our study. Previous reports have included older subjects than those described here, so the difference in triglycerides may develop with increasing age. Likewise, blood pressures, reported as elevated[23] or reduced[7] in UK-resident South Asian females, were found not to differ significantly from those of white females in this study. Again, age-related differences may be important.

Females in the black group displayed fasting hyperinsulinemia and an elevated insulin response to glucose as compared with white females. This was associated with lower serum triglyceride and glucose indices, indicating that elevated insulin levels in these subjects were not due to insulin resistance. Furthermore, black females displayed levels of serum lipid metabolic risk markers consistent with a decreased risk of CHD. Improved glucose tolerance relative to whites has been observed in US blacks,[32] but not in Afro-Caribbeans compared with white UK residents.[10,33] The higher prevalence of glucose intolerance in immigrant black populations[33] and the utilization of older and type II diabetic subjects in such studies both limit comparison with our study. Lower serum triglyceride and higher HDL cholesterol levels than found in whites have been reported in US black men.[34,35] US black women show trends similar to white women in terms of triglyceride and HDL cholesterol, although the differences are less marked and not consistently statistically significant in the studies.[35,36] In the United Kingdom, lower triglyceride and higher HDL cholesterol have been reported in Afro-Caribbeans as compared with whites,[33,37] but this is not a universal finding.[10] Despite hyperinsulinemia, blood pressures in blacks did not differ significantly from those in whites, in accordance with a previous UK study of white and black workers of both sexes.[38]

Oriental females showed elevated insulin levels as compared with whites, but not before standardization for age and BMI. The Oriental women we studied were older and of lower BMI than the whites, and consequently, characteristics of the groups we compared may have obscured an underlying difference in insulin metabolism. We are unaware of any other cross-sectional studies investigating levels of CHD risk markers in immigrants to the United Kingdom from Oriental countries, or levels of cardiovascular mortality or type II diabetes prevalence within this group. Immigration of Japanese men to the United States is

associated with increases in serum total cholesterol, glucose, and triglyceride[39] and an elevated prevalence of glucose intolerance in both male and female immigrants.[40] Chinese residing in Mauritius have an elevated prevalence of glucose intolerance[41] and higher total cholesterol and non-HDL cholesterol than Beijing-resident Chinese.[2]

Duration of residence in the United Kingdom for the immigrant groups was not associated with consistent changes in levels of metabolic risk markers or blood pressure. This accords with a study of UK female factory workers of West Indian and Asian origin.[38] However, the study design would not have identified any changes that occurred within 1 year of immigration.

SES is a possible confounder of the study findings, since blood lipid levels are associated with measures of SES in various ethnic groups.[42,43] Although data pertaining to the SES of these women were not available, we consider it unlikely that SES explains the intergroup differences seen, since the subjects, regardless of racial group, were recruited from comparable sources.

We do not have data concerning diet. Findings of a lower quantity of fat purchased per person[44] and of both a lower fat intake, as a percentage of dietary energy, and a higher dietary polyunsaturated to saturated fat ratio in UK-resident blacks as compared with whites[9] are consistent with the suggestion that diet may partially explain intergroup differences in lipids. However, similar intergroup differences have been noted in men after 2 years' feeding of a Western diet.[45] The dietary polyunsaturated to saturated fat ratio appears to be greater in UK-resident South Asians as compared with whites,[9,24] whereas the percentage of dietary fat intake may be similar[9] or greater[46] in the former group. However, Indian and white women consuming diets similar in protein, fat, and carbohydrate composition exhibit differences in lipids and lipoproteins[47] comparable to those described by us, and thus it is unlikely that diet alone explains intergroup differences reported here.

In the present study, only BMI was used as an index of adiposity in these non-obese females. Body fat distribution may be particularly important as a factor underlying ethnic differences in CHD metabolic risk markers.[23,37] Potentially adverse associations of central obesity with lipid metabolic risk factors for CHD and blood pressure, previously documented in white populations, have also been observed in US-resident blacks,[48] UK-resident South Asians,[23] and Japanese men.[49] These findings together with observations of differences in fat distribution indices between UK-resident white and non-obese South Asian[50] and between US white and black women[48] underscore fat distribution as a potential confounder of the study findings. The use of an index related to fat distribution, validated for use in the racial groups studied, might have provided further insight into the factors underlying the differences we observed.[27]

Clearly, healthy non-obese UK-resident premenopausal females of various racial origins differ in levels of metabolic CHD risk markers, in ways that are consistent with the relative prevalence of CHD within the groups. Additionally, our findings suggest that there are differences in the associations between metabolic variables in the groups studied. However, we cannot ascribe these differences to either genetic or life-style influences with this study design. It is noteworthy that these differences are found between healthy young females, who are thought to have the least risk for CHD in comparison to the general population. More study is needed to assess the clinical significance of these differences and their relation to diet and life-style factors in the etiology of CHD and when developing a relevant CHD preventative strategy for a particular community.

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