CARDIOVASCULAR MEDICINE

Risk factors for non-fatal myocardial infarction in young South Asian adults

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Objective: To determine the risk factors for premature myocardial infarction among young South Asians.
Design and setting: Case–control study in a hospital admitting unselected patients with non-fatal acute myocardial infarction.
Methods and subjects: Risk factor assessment was done in 193 subjects aged 15–45 years with a first acute myocardial infarct, and in 193 age, sex, and neighbourhood matched population based controls.
Results: The mean (SD) age of the subjects was 39 (4.9) years and 326 (84.5%) were male. Current smoking (odds ratio (OR) 3.82, 95% confidence interval (CI) 1.47 to 9.94), use of ghee (hydrogenated vegetable oil) in cooking (OR 3.91, 95% CI 1.52 to 10.03), raised fasting blood glucose (OR 3.32, 95% CI 1.21 to 8.62), raised serum cholesterol (OR 1.67, 95% CI 1.14 to 2.45 for each 1.0 mmol/l increase), low income (OR 5.05, 95% CI 1.71 to 14.96), paternal history of cardiovascular disease (OR 4.84, 95% CI 1.42 to 16.53), and parental consanguinity (OR 3.80, 95% CI 1.13 to 1.75) were all independent risk factors for acute myocardial infarction in young adults. Formal education versus no education had an independently protective effect on acute myocardial infarction (OR 0.04, 95% CI 0.01 to 0.35).
Conclusions: Tobacco use, ghee intake, raised fasting glucose, high cholesterol, paternal history of cardiovascular disease, low income, and low level of education are associated with premature acute myocardial infarction in South Asians. The association of parental consanguinity with acute myocardial infarction is reported for the first time and deserves further study.

Cardiovascular disease is a major global health problem reaching epidemic proportions.[1] Low and middle income countries, including the South Asian countries of India and Pakistan, contribute significantly to the global burden of cardiovascular disease, accounting for 78% of all deaths and 86.3% of all loss of disability adjusted life years attributable to this cause.[2]

High risks of cardiovascular disease have been reported in South Asian populations, regardless of whether they live overseas or in their native countries.[2–7] Epidemiological studies show that migrant populations of South Asian descent have higher risks of ischaemic heart disease than the native population.[4 8] Moreover, coronary artery disease tends to emerge earlier in life, and thus mortality rate ratios are greatest in the youngest South Asians compared with other ethnic groups.[8 9] However, acute myocardial infarction in young South Asians has not been extensively studied, and most of the existing data are on migrant South Asian populations. Furthermore, studies of migrant South Asians have focused on explanations for between-population differences, such as triglyceride and insulin resistance, rather than determining important risk factors within that population, which are not the same but are critical when considering disease prevention policies. We therefore conducted a case–control study of young individuals (aged 15–45 years) with a first myocardial infarct in Karachi, Pakistan, to determine the risk factors and the relative importance of these factors for acute myocardial infarction among young South Asians.

METHODS

Subjects

Cases

With their informed consent, we prospectively enrolled 193 consecutive patients aged 15–45 years who were admitted to the coronary care units of the National Institute of Cardiovascular Diseases and Liaquat National Hospital with acute myocardial infarction. Myocardial infarction was defined by the presence of at least two of the following[10]:

- typical chest pain lasting at least 20 minutes
- an ECG showing ST elevation of at least 2 mm in two or more contiguous leads, with subsequent evolution of the changes
- diagnostic enzyme changes (doubling of creatine kinase with at least 10% MB fraction).

Patients were excluded if they had a history of heart disease, clinical evidence of liver disease, were incapable of giving consent, or died within 24 hours of incident acute myocardial infarction. All cases were enrolled between August 2001 and June 2002.

Controls

An identical number of controls were selected from the neighbourhood of each case, after matching for age ($\pm$5 years) and sex. The selection method involved identifying the house of the case subject and then flipping a coin to determine whether to turn right or left. The third house in the block adjacent to the case subject's house on the selected side was screened for an eligible control subject. If no control was found, adjacent houses were screened sequentially until an eligible control subject was recruited, after obtaining informed consent. Subjects were excluded if they had angina (Rose questionnaire); if they had history, clinical evidence, or ECG evidence of heart disease; if there was clinical evidence of liver disease; or if they were incapable of giving consent.

Variables

A detailed standardised questionnaire was developed using standard methods. In all participants, we recorded data on sociodemographic characteristics such as age, sex, marital status, occupation, monthly income, educational level, dietary pattern (based on food frequency questionnaire), physical activity, tobacco use, family history of heart disease, diabetes, consanguineous marriages, and known history of hypertension and diabetes. Anthropometric measurements including height, weight, waist circumference, and hip circumference were obtained. Waist circumference was measured at the narrowest diameter between the costal margin and the iliac crest. Hip circumference was measured at the greatest diameter over the buttock. Two readings of blood pressure were recorded in the supine position with a mercury sphygmomanometer. An ECG was done in all participants. Trained research assistants carried out all measurements using standardised protocols.

Fasting blood glucose and lipids were measured within 24 hours of admission of the case subjects, and in all control subjects. Blood samples of all participants were sent to the Aga Khan University Hospital laboratory.

Ethical approval was obtained from the ethics review committee, Aga Khan University, Karachi.

Statistical analysis

Comparison of continuous (mean) and discrete variables was done between cases and controls. Stepwise conditional logistic regression analysis was carried out using forward selection with inclusion probability (p) value of 0.2, after matching of cases with controls for continuous variables (body mass index, waist-hip ratio, systolic and diastolic blood pressures, and fasting blood cholesterol) and for categorical variables (current smoking, proportion with raised blood glucose (fasting blood glucose $\geqslant$ 6.1 mmol/l),[11] history of diabetes, hypertension, education status, income level, use of ghee (clarified butter) in cooking, meat consumption, physical activity, parental consanguinity, and paternal and maternal history of cardiovascular disease). Estimates of odds ratios (OR) and 95% confidence intervals (CI) were made. Interaction terms between variables were tested for significance. SAS statistical software (SAS Institute Inc, Cary, North Carolina, USA) was used for all analyses. Probability values were two tailed.

RESULTS

The response rate was 100% for cases and 96.5% for controls. In all, 388 subjects were recruited (194 cases and 194 controls). One patient died on the third day of admission before complete data were obtained, and so one subject each from the case and control groups was excluded from the analysis.

The demographic characteristics of the subjects are shown in table 1. Their mean (SD) age was 39 (4.9) years (range 15–45 years) and 84.5% were male. Compared with the controls, cases were more likely to use ghee (hydrogenated vegetable oil) in cooking (54.4% *v* 21.2%, $p = 0.001$), to smoke (51.8% *v* 21.2%, $p = 0.001$), to have parents who were also first cousins (parental consanguinity) (34.2% *v* 18.6%, $p = 0.001$), to have a lower income (73.6% *v* 50.6%, $p = 0.001$), to have a lower education level (5.1% *v* 31.6%, $p = 0.001$ had formal school education), to have a raised blood glucose (38.9% *v* 24.4%, $p = 0.001$), and to have raised mean cholesterol concentrations (5.1 *v* 4.5 mmol/l, $p < 0.001$).

The unadjusted odds ratios (with 95% confidence intervals) for factors associated with acute myocardial infarction are shown in table 2. In the univariate analyses, current smoking, raised blood glucose, raised blood cholesterol, parental first cousin marriage, use of ghee in cooking, lack of education, and low income level ($p < 0.001$ for each), and paternal history of myocardial infarction ($p = 0.03$), were all associated with a higher risk of acute myocardial infarction.

Table 3 shows a comparison of smoking characteristics between the cases and the controls. In all, 141 subjects (36.5%) were current smokers: 100 (51.8%) in the case group and 41 (21.2%) in the control group ($p = 0.001$). There was a higher proportion of heavy smokers ($\geqslant$ 10 cigarettes a day) among cases than controls (36.8 *v* 10.4%). The average age at which subjects started smoking was younger in cases than in controls (18.8 *v* 21.9 years, respectively, $p < 0.001$).

The predictive independent variables identified in the stepwise multivariate conditional regression analysis were: lack of education ($p < 0.001$); use of ghee in cooking ($p < 0.001$); raised blood glucose ($p < 0.001$); current smoking ($p = 0.001$); low income ($p = 0.002$); raised blood cholesterol ($p = 0.005$); paternal history of cardiovascular disease ($p = 0.01$); and first cousin marriage ($p = 0.04$). The adjusted odds ratios (95% CI) for factors associated with acute myocardial infarction are shown in table 2.

No significant interactions were detected among the variables for risk of acute myocardial infarction. Analysis was repeated using unmatched logistic regression analysis. The overall results remained unchanged.

DISCUSSION

This is the first reported case–control study aimed at identifying the risk factors for acute myocardial infarction in young South Asian adults ($\leqslant$ 45 years) from Karachi. We found that smoking, the use of ghee in cooking, raised blood glucose and cholesterol, parental consanguinity, paternal history of cardiovascular disease, low level of income, and lack of education were all independent risk factors for acute myocardial infarction in young South Asian adults.

Our study was conducted in institutions which are renowned for providing first line cardiac care to urban and suburban populations from all socioeconomic strata in Karachi, the most populous city of Pakistan. Our criteria for the diagnosis of acute myocardial infarction were stringent and the cases were not known to have had previous heart disease. This avoids the possibility of misdiagnosis of cases identified by the sole use of ECG. Further, our method of randomly selecting age and sex matched controls from the residential neighbourhoods of the case subjects minimises selection bias and reduces confounding by other identified and unidentified factors related to socioeconomic status.

Population surveys indicate that around two thirds of marriages in Pakistan are consanguineous.[12 13] There are controversial data on whether consanguineous marriages lead to a higher incidence of congenital and acquired diseases in the offspring.[14 15] Our study is the first to report a relation between parental consanguinity and early myocardial infarction, independent of family history of cardiovascular disease. It is reasonable to speculate that consanguinity increases the likelihood of inheriting genetic factors—identified as well as unidentified—leading to premature ischaemic heart disease. However, environmental factors such as dietary patterns are more likely to be shared among family members, and this effect will probably be stronger in consanguineous relationships. Further studies are needed to confirm this. If found to be true, one could speculate that consanguinity has a confounding effect on the risk factors thought to be specific to the South Asian population.

Countries like India, Pakistan, and Bangladesh, where consanguineous marriages are very common (15–66%), are home to over one sixth of the world's population.[12 13 16 17] These countries are major contributors to the global burden of cardiovascular disease at present, and their contribution is projected to grow, given their consistent population growth rates.[1] Furthermore, the practice of consanguinity is also observed in migrant South Asian populations in the West as well as in native populations in the Middle East,[18] China,[19]

Table 1 Comparison of characteristics between cases and controls

Variable	Total	Cases	Controls	p Value
Number of patients	386	193	193	
Male	326 (84.5%)	163 (84.5%)	163 (84.5%)	0.99
Age (years)	39.0 (4.9)	39.3 (5.1)	38.7 (4.7)	0.29
Weight (kg)	69.3 (12.7)	68.9 (12.5)	69.8 (12.9)	0.51
Body mass index (kg/m^2)	24.9 (4.7)	24.9 (4.4)	24.8 (5.0)	0.97
*Overweight	178 (46.1%)	97 (50.3%)	81 (41.9%)	0.10
†Obese	39 (10.1%)	21 (10.9%)	18 (19.3%)	0.61
Waist-hip ratio	0.93 (0.1)	0.93 (0.1)	0.93 (0.1)	0.97
Systolic BP (mm Hg)	120.1 (17.1)	118.5 (18.1)	122.6 (15.9)	0.02
Diastolic BP (mm Hg)	78.3 (17.2)	78.1 (22.0)	78.6 (10.5)	0.77
Fasting blood glucose (mmol/l)	7.2 (4.2)	8.1 (5.2)	6.6 (3.2)	0.001
‡Raised blood glucose	122 (31.6%)	75 (38.9%)	47 (24.4%)	0.001
Serum cholesterol (mmol/l)	4.8 (1.9)	5.1 (1.3)	4.5 (1.0)	<0.001
§Raised blood cholesterol	112 (30.2%)	75 (38.9%)	37 (19.2%)	0.001
Illicit drug use	14 (3.7%)	8 (4.2%)	6 (3.2%)	0.60
Ghee in cooking	146 (37.8%)	105 (54.4%)	41 (21.2%)	0.001
¶Beef or mutton eaters	320 (82.9%)	165 (85.5%)	155 (80.3%)	0.18
**Parental consanguinity	102 (26.4%)	66 (34.2%)	36 (18.6%)	0.001
††Paternal history of CVD	80 (21.2%)	48 (24.9%)	32 (16.6%)	0.05
††Maternal history of CVD	83 (22.1%)	44 (22.8%)	39 (20.2%)	0.47
History of hypertension	61 (15.8%)	27 (14.0%)	34 (17.7%)	0.21
History of diabetes	37 (9.6%)	13 (6.7%)	24 (12. %5)	0.06
‡‡Monthly income $\leqslant$Rs 5000	239 (61.9%)	142 (73.6%)	97 (50.3%)	0.001
Level of education				0.001
None	71 (18.4%)	61 (31.6%)	10 (5.1%)	
School	198 (51.3%)	96 (49.8%)	104 (52.9%)	
College	117 (30.3%)	36 (18.7%)	84 (42.4%)	
§§Exercise	67 (17.4%)	41 (21.2%)	26 (13.5%)	0.05
Married (%)	341 (88.5)	170 (88.1)	171 (89.1)	0.85

Values are n (%) or mean (SD). Comparison of variables between cases and controls was done using the *t* test for continuous variables and the χ^2 test for discrete variables.
*Overweight defined as BMI >25 kg/m^2.
†Obesity defined as BMI $\geqslant$30 kg/m^2.
‡Raised blood glucose defined as fasting blood glucose $\geqslant$6.1 mmol/l (110 mg/dl).
§Raised blood cholesterol defined as total cholesterol $\geqslant$5.18 mmol/l (200 mg/dl).
¶Meat consumption is defined as intake of beef and mutton or not.
**Parental consanguinity is defined as first cousin marriage between parents of subjects.
††2.8% and 2.3% of subjects did not know about paternal and maternal history of cardiovascular disease, respectively.
‡‡US $1 = 60 Pakistan rupees (Rs)
§§Exercise was defined as jogging, swimming, bicycling, or exercising in the gymnasium most days of the week during the past six months.
BMI, body mass index; BP, blood pressure; CVD, cardiovascular disease.

Turkey,[20] and Africa.[21] The association of consanguinity and premature heart disease needs to be studied in these populous nations as well as in cross-population ethnic studies.

Our study highlights the relative importance of potentially modifiable risk factors for acute myocardial infarction in the young population of Pakistan. Smoking—an established risk factor for acute myocardial infarction—is associated with endothelial dysfunction and can precipitate coronary spasm.[22] Thus smoking can contribute to myocardial infarction even in subjects with minimal atherosclerosis. In our study, the odds ratio for acute myocardial infarction in current smokers was 3.82 (95% CI 1.47 to 9.94) compared with current non-smokers. As shown in table 3, the risk was higher in those who smoked heavily. Further, there was a significant difference in the age of initiation of smoking between cases (18.8 years) and controls (21.9 years) ($p < 0.001$). Owing to increased restrictions in the industrialised countries, the marketing strategies of tobacco companies are now targeting the adolescent population in developing countries.[23 24] Our findings emphasise the need for antitobacco campaigns to target children and young adults, and strict legislation against advertising cigarettes for this vulnerable population.

Saturated fat intake has been related to acute myocardial infarction in adults.[25] Ghee contains cholesterol oxides that are thought to be related to atherosclerosis.[26] In adipose tissue of subjects who use ghee for cooking compared with other types of non-hydrogenated oils, a higher percentage of *trans* fatty acids, known to increase the risk of ischaemic heart disease,[27] has been reported.[28] Although previous studies in South Asian populations indicate a high consumption of ghee in India and Pakistan, data for an independent relation between ghee and cardiovascular disease in the same population are conflicting.[7 29 30] The production of ghee has been rising sharply in Pakistan.[31 32] Ours is the first study to show an independent association between ghee consumption and acute myocardial infarction. We found a high risk of infarction in young Pakistani adults attributable to ghee (adjusted relative risk 3.92, 95% CI 1.52 to 10.03). A high prevalence of ghee consumption has also been reported in migrant South Asians living in the West.[33] Our findings suggest that ghee consumption is a potential target for preventive strategies.

The association between a low level of education and acute myocardial infarction has been reported previously in other populations.[34 35] It is speculated that high risk behaviours contributing to cardiovascular disease are more common in individuals with low levels of education.[36] We found that subjects who did not attend school were at higher risk of acute myocardial infarction than those who did. Our findings also suggest that this association is not entirely related to the conventional risk factors including smoking, ghee, low income, and level of physical activity. Thus other psychosocial behaviours associated with lack of education are likely to be responsible for this relation.

Table 2 Unadjusted and adjusted risk of acute myocardial infarction

	Unadjusted odds ratio (95% CI)	*Adjusted odds ratio (95% CI)
Current *v* non-current smoker	4.22 (2.53 to 7.06)	3.82 (1.47 to 9.94)
Ghee *v* no ghee in cooking	4.94 (2.89 to 8.45)	3.91 (1.52 to 10.03)
†Raised *v* normal blood glucose	4.00 (2.27 to 7.04)	3.23 (1.21 to 8.62)
Blood cholesterol	1.57 (1.28 to 1.93), for each 1.0 mmol/l increase	1.67 (1.14 to 2.45), for each 1.0 mmol/l increase
Mean systolic blood pressure	1.02 (1.00 to 1.03)	‡NS
Mean diastolic blood pressure	1.00 (0.99 to 1.01)	NS
§Parental consanguinity *v* no consanguinity	2.43 (1.46 to 4.04)	3.80 (1.13 to 12.75)
Formal schooling *v* no school	0.06 (0.02 to 0.17)	0.04 (0.01 to 0.35)
Consume meat	1.50 (0.85 to 2.64)	NS
Monthly income less than *v* more than Rs 5000	1.81 (1.06 to 3.08)	5.05 (1.71 to 14.96)
Body mass index	1.00 (0.96 to 1.05), for each unit increase	NS
Waist-hip ratio (SD)	0.97 (0.07 to 13.13), for each unit increase	NS
Illicit drug use	0.75 (0.26 to 2.16)	NS
Paternal history of CVD *v* no paternal history of CVD	1.81 (1.06 to 3.08)	4.84 (1.42 to 16.53)
Maternal history of CVD *v* no maternal history of CVD	1.17 (0.72 to 1.90)	1.33 (0.43 to 4.08)
History of hypertension *v* no history of hypertension	0.67 (0.38 to 1.17)	NS
History of diabetes *v* no history of diabetes	0.50 (0.24 to 1.03)	NS
¶Exercise *v* no exercise	1.75 (1.01 to 3.03)	1.89 (0.52 to 6.85)
Married *v* unmarried	1.00 (0.51 to 1.96)	NS

*Adjusted odds ratios are based on multivariable model.
†Raised blood glucose defined as fasting blood glucose ⩾6.1 mmol/l (110 mg/dl).
‡NS: these factors were not significantly associated with acute myocardial infarction in the multivariable model and were therefore not included in the final model.
§Parental consanguinity is defined as first cousin marriage between parents of subjects.
¶Exercise was defined as jogging, swimming, bicycling or exercising in the gymnasium most days of the week during the past six months.
CI, confidence interval; CVD, cardiovascular disease.

We did not find a correlation between central obesity, meat consumption, physical inactivity, and acute myocardial infarction.[37] It is possible that the broad prevalence of these risk factors in the entire study population limited their recognition as an aetiological agent in a population study.[38] It is also important to emphasise that failure to detect an association between these risk factors and acute myocardial infarction in a young South Asian population does not mean that these are not important factors in South Asians compared with other populations.

Our study has various limitations. We did not measure all the possible risk factors for acute myocardial infarction, such as the fractionated lipid profile, emerging risk factors like serum homocysteine and fibrinogen concentrations, and psychosocial factors such as stress and anger.[36 39] However, we did measure blood cholesterol and most other modifiable conventional risk factors for acute myocardial infarction. Further, as compared with other populations, people of South Asian descent are known to have an excess of certain cardiovascular risk factors such as insulin resistance and abnormal triglyceride values.[40] However, that does not necessarily translate into a South Asian group effect. We do not believe that our findings are biased by failure to account for these factors, though they would, no doubt, be important to examine in a study comparing populations.

We did not detect any interactions between the factors associated with risk of acute myocardial infarction. Studying these factors in a much larger sample could shed more light on the possible complex interrelations among them. However, our study has the largest sample of young South Asians with acute myocardial infarction reported so far. The study was not designed to estimate the proportion of patients who die within 24 hours of acute myocardial infarction, or to study the risk factors associated with fatal acute infarction. However, the high response rate in our study increases the likelihood of our results being generalisable to patients with non-fatal acute myocardial infarction. Finally, while this study does not establish a cause–effect relation between the

Table 3 Smoking and the risk of acute myocardial infarction

Variable	Total	Cases	Controls	*Unadjusted odds ratio (95% CI)
Never smoked	207 (53.6)	69 (35.8)	138 (71.5)	1.00
Former smoker	38 (9.7)	24 (12.4)	14 (7.3)	5.89 (2.43 to 14.27)
Current smoker	141 (36.5)	100 (51.8)	41 (21.2)	6.85 (3.66 to 12.81)
1–10 cigarettes/day	37 (9.5)	17 (8.8)	20 (10.4)	1.89 (0.87 to 4.09)
>10 cigarettes/day	91 (23.3)	71 (36.8)	20 (10.4)	6.44 (3.36 to 12.35)
Age (years) when started smoking	19.7 (5.7)	18.8 (5.6)	21.9 (6.1)	0.73 (0.57 to 0.95) for each year increase in age

Values are n (%).
*Odds ratios for acute myocardial infarction were computed using logistic regression after matching cases with controls. Reference group was never-smokers (never smoked at any time).

identified risk factors and premature heart disease, it raises the possibility that several of the associated factors may be modifiable risk factors for acute myocardial infarction.

Based on our findings, we suggest that stringent tobacco control programmes, legislation to restrict the production of ghee, the promotion of exercise and other lifestyle and dietary measures to improve glucose tolerance,[41] cholesterol screening programmes, and improving the level of education are likely to have a profound effect on the burden of premature ischaemic heart disease in South Asians. The relation between parental consanguineous marriages and acute myocardial infarction needs further study.

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