Objective: We assessed the distribution of coronary artery disease (CAD) and its association with the major biological risk factors and behaviors among Pakistanis presenting at a tertiary care hospital in Karachi, Pakistan.

Method: An epidemiologic cross-sectional study was conducted at the Aga Khan University Hospital (a teaching hospital) in Karachi, Pakistan. A total of 600 adult (\geq 18 years of age) patients visiting family practice clinics for general check-up were included. The association of biological risk factors with CAD (smoking, obesity [body mass index (BMI)], hypertension, family history of ischemic heart diseases [IHD], sedentary lifestyle, diabetes mellitus, total cholesterol, low density lipoprotein [LDL] levels, high density lipoprotein [HDL] levels, and triglycerides) were assessed.

Results: On univariate analysis, age \geq 40 years, early menopause, BMI \geq 29.9 kg/m², diabetes, high cholesterol, and positive family history of IHD were independently associated with CAD. We found age \geq 40 years, diabetes, and positive family history of IHD strongly related with CAD on multivariate analysis.

Conclusion: Looking at the strong association of major risk factors with CAD, the unique characteristics of Pakistanis must be studied in depth, with focus on high-risk groups. (*Ethn Dis.* 2005;15:429–435)

Key Words: Coronary Artery Disease, Developing Countries, Hypertension, Risk Factors

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INTRODUCTION

As epidemiologic transition accompanies socioeconomic and demographic changes, the epidemic of cardiovascular disease (CVD) is accelerating in developing countries.1 In the year 2000, 16.7 million people died from CVD, accounting for 30.3% of all deaths worldwide, and >40% of these deaths are from the developing countries.1 This epidemiologic transition in developing countries is due to several causes.² Although decline in mortality rates have occurred in most industrialized countries, increase has been seen in developing countries. Our knowledge of risk factors for acute myocardial infarction (AMI) is largely derived from studies in industrialized nations.

South Asians (people from Pakistan, India, and Bangladesh) have among the highest rates of coronary artery disease (CAD). These rates have been recorded in studies of expatriate South Asians^{3–7} and have also been shown in native settings.^{8,9}

Smoking, hypertension, dyslipidemia, diabetes, and sedentary lifestyle are associated with CAD^{9–12}; however, little information exists concerning risk factors of CAD in developing countries, and virtually none has come from Pakistan. Whether the conclusions derived from these studies may be extrapolated to people in developing countries of different ethnic backgrounds is unclear.

The epidemic of CHD appears to emerge first in higher socioeconomic groups and second in lower socioeconomic classes.^{13,14} Hence, the stage of development of any given society in this epidemiologic transition would influence the distribution of CAD.¹⁵

Pakistan is a developing country with >140 million persons in its four

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provinces.¹⁶ Though most Pakistanis are poor, approximately 10% belong to the upper socioeconomic class. Limited hospital- and population-based studies in Pakistan focus on CAD and its risk factors, and many existing studies have obvious limitations. The National Health Survey of Pakistan (NHSP)17 is the first community survey providing data on health problems prevailing in Pakistan; this survey collected limited information on CAD and its determinants. Available data on CAD risk factors in NHSP showed a high prevalence of risk factors in urban and rural poplutions,¹⁷ but this information is neither complete nor satisfactory with respect to CAD. In addition, insufficient data are available in the upper socioeconomic class of Pakistanis, a class more susceptible to CAD and its determinants and considered to be "early adopters" and a high-risk group.

The purpose of the study was to assess the distribution of CAD and its association with the major biological risk factors and behaviors among upper- and middle-upper-class Pakistanis attending general preventive checkup clinics at a teaching hospital in Karachi, a city of Pakistan.

Method

In this cross-sectional study, a convenience sample of 600 Pakistani patients, which was representative of higher socioeconomic classes, who visited the Aga Khan University Hospital (AKUH) for a checkup was surveyed from March 2001 to February 2002. The AKUH facility is a private teaching hospital in Pakistan and caters to all segments of society. These clinics provide checkups to upper-middle- and upper-

South Asians (people from	Table 1. Criteria for risk factors used in the study			
Dahistan India and	Variable		Definition	
Bangladesh) have among the	Hypertension ¹⁸ (JNC VI classification)	A systolic blood pressure of ≥140 mm Hg and/or a diastolic blood pressure ≥90 mm Hg on examination		
highest rates of coronary artery disease (CAD).	BMI ¹⁹	BMI=weight (kg)/h <18.5 18.5–24.9 kg/m ² ≥25.0 kg/m ² 25–29.9 kg/m ² 30.0–34.9 kg/m ² 35.0–39.9 kg/m ² ≥40 kg/m ²	neight (m ²) = Underweight = Average = Overweight (divided into 4 groups) = Pre-obese = Moderate (obese class I) = Severe (obese class II) = Very severe (obese class III)	
class populations and are run by trained family physicians. All patients aged ≥ 18 years attending these clinics were in-	Positive IHD family history ²⁰	CAD in a first-degree male relative (grandfather, father, or brother) before the age of 55 years or first-degree female ative (grandmother, mother, or sister) before 65 years		
cluded in the study. In all patients, age, sex, educational level, language, family size, and income level were recorded in addition to other demographic variables. Information on smoking, hypertension, family history of IHD, sedentary life- style, fasting blood glucose and lipids (total, low-density lipoprotein [LDL] and high-density lipoprotein [HDL] cholesterol, and triglycerides) were ob-	Smoking ²¹ Current regular smoker Occasional smoker Ex-smoker Never smoked Sedentary lifestyle ²² Diabetes mellitus ²³	 Smoke one or more cigarette per day, everyday Smokes less than 3–4 cigarettes per wk or in social gathering Does not smoke at the present time, but has smoked daily in the past Does not smoke at present time and never smoked in the pa Defined as less than three episodes of physical activity of less than 20 minutes per week in last 4 weeks before interview Two fasting plasma glucose levels of ≥126 mg/dL (≥7.0 mm L) or patients on oral hypoglycemic drugs and/or taking inst 		
tained. Data were recorded on a ques- tionnaire prepared by the authors, which was developed in Urdu (Pakistan's national language) and was pretested in	Serum cholesterol ²⁴ (NCEP ATP III classification*) * LDL, HDL, and triglycerides acc	<20 mg/dL (5.2 m 200–239 mg/dL (5 >240 mg/dL (≥6.3 ording to NCEP ATP III.	nmol/L)—Desirable .2–6.19 mmol/L)—Borderline High 2 mmol/L)—High	

Criteria for risk factors used in the study Tabla 1

us the largest sample size possible, and 600 patients constituted our sample for the study.

Data Analysis

The SAS (SAS institute, Cary, NC) statistical package was used for data entry and analysis. Descriptive statistics described basic features of the data in our study, such as means and standard deviations. The data were normally distributed, so we did not use nonparametric tests. The univariate and multivariate logistic regression analyses were used to assess the association between CAD and its risk factors and risk behaviors. Adjustments for possible confounders were made by including in the multivariate model age, BMI, diabetes, hypertension, family history of IHD, sedentary lifestyle, and cholesterol. For

the age variable in univariate and multivariate analysis, we took 40 years as a cutoff value. Similarly for LDL and HDL, analysis was performed by using 100 mg/dL and 40 mg/dL as cutoff values, respectively. Results were expressed as odds ratios (OR) and 95% confidence interval (CI).

Ethics Approval

The proposal was submitted to and approved by the hospital ethics committee of the Aga Khan University. Prior to data collection, consent was obtained from all the family physicians for patient recruitment in the study. In addition, written consent was obtained from the participants after informing them about the risks and benefits related to the study. No subject has been identified in any report or publication.

Keeping in mind the previous available limited data on CAD and its risk factors in Pakistan,^{8,26} we assumed the prevalence of CAD risk factors to be 50% with \pm 5% margin of error to give

patients similar in socioeconomic standing to the actual study sample. Risk factors were defined according to definitions given in Table 1. Coronary artery

disease (CAD) was diagnosed in our

study sample if patients satisfied ≥ 1 of

the following criteria: history of docu-

mented myocardial infarction (MI), an-

giographically documented CAD, or

history of typical exertional angina pec-

toris with a positive exercise treadmill

test with or without nuclear imaging. In

the absence of angina pectoris, previous

angiography, or MI, abnormal exercise

treadmill test results with abnormal im-

aging findings confirmed the presence

of CAD.25

Variable	N=600	%
Age group	46.1*	10.2†
18–34	73	12.2
35–64	513	85.5
65+	14	2.3
Gender		
Male	471	78.5
Female	129	21.5
Monthly income		
<rs 5000<="" td=""><td>21</td><td>3.5</td></rs>	21	3.5
Rs 5000–Rs 12,000	45	7.5
Rs 12.000–Rs 40.000	98	16.3
>Rs 40.000	355	59.1
Refused	81	13.5
Employment status		
Full time (≥35 hr/wk)	410	68.3
Unemployed	5	0.8
Retired/student	60	10
Household person	115	19.2
Refused	3	0.5
Work type		
Professional	49	11.2
Clerical	16	3.8
Skilled foreman	26	6.2
Manager/official/proprietor	316	75.8
Sales worker	7	1.7
Non skilled	2	0.5
Refused	1	0.2
Missing	183	
Language		
Urdu	286	47.7
Sindhi	81	13.5
Punjabi	124	20.7
Pushto	39	6.5
Baluchi	29	4.8
Others	41	6.8
Education		
Never matriculated	12	2.0
Matriculate	51	8.5
Intermediate	104	17.3
Graduate	389	64.8
Post-graduate	44	7.3

Table 2. Sociodemographic variables in the study group

RESULTS

The demographic characteristics of patients are shown in Table 2. Mean age was 46 (\pm 10.2) years, and most were males (78.5%), with the largest number in the 35- to 64-year age category. To present the patients from the four provinces of Pakistan (Sindh, Punjab, Balu-

chistan, and Northern Western Frontier Province), language was used as a surrogate marker of ethnicity for five ethnic groups in our study sample. Urduspeaking people (those who migrated from India) made up 47.7% of the sample. Most of this study group belonged to upper and upper-middle socioeconomic classes, and 47.3% had a monthly income >Rs 400,000 (>US\$1000). The study group was well educated, and 64.8% were college graduates.

Coronary Artery Disease and its Determinants

Coronary artery disease (CAD) was reported in 19% of patients (Table 3). The most striking findings was a positive family history of IHD seen in 48%. Only a few patients had triglycerides \geq 400 mg/dL (3.7%). Most patients were not involved in regular exercise (71.8%). Among females, 50% were menopausal, and mean age at menopause was 46.6 years (± 5.2).

We found on univariate analysis, age \geq 40 years, early menopause in women, BMI \geq 29.9 kg/m², diabetes, high cholesterol, and positive family history of IHD to be independently associated with CAD (Table 4). Furthermore, on multivariate analysis, age \geq 40 years, diabetes, and positive family history of IHD were strongly associated with CAD (Table 5).

DISCUSSION

In this cross-sectional study of upper class Pakistanis, age, diabetes, and positive family history of IHD were strongly associated with CAD. The study sample was from different parts of urban Karachi, and the subjects belonged to uppermiddle and higher socioeconomic classes. That the risk of CAD is higher in patients with diabetes mellitus is well known.10 Although, this study was not designed to estimate the risk of CAD conferred by diabetes, the observation of a high proportion of diabetes in subjects with CAD (OR=1.77, 95% CI 0.99-2.87) confirmed the association of CAD with diabetes as seen in other studies14,29,30; however, the association is not strong. One reason could be the design of the study and patient selection. Most studies that have found a strong association of risk factors had case-control designs. This study is a cross-section-

Table 3. CAD and its risk factors in study group

Variable	N=600	%
CAD		
Positive	115	19.1
Negative	485	80.9
Menopause (n=129)	46.6*	5.2†
Yes	64	50.4
INO .	65	49.6
BMI categories	28.2*	14.7†
Underweight (<18.5) Normal (18.5–24.9)	5 172	0.8
Pre-obese (25–29.9)	290	48.4
Obese class I and II (30-39.9)	123	20.6
Obese class III (≥40)	9	1.5
Refused	I	0.1
Diabetes	0.0	16.0
No	98 473	78.8
IGT‡	29	4.8
Hypertension		
Yes	121	20.2
No	479	79.8
Total cholesterol	194.2*	37.2†
Desirable (<200)	402	67.0
Borderline high $(200-239)$ High (>240)	118 80	19./
	20.9*	7.0+
L_{OW} (<40)	300	50.0
40–59	292	48.7
High (≥60)	8	1.3
LDL cholesterol	124.5*	32.2†
Optimal (<100)	113	18.8
Near/above optimal (100–129) Rorderline high (120–159)	228	38.0
High (160–189)	71	11.8
Very high (≥190)	11	1.8
Triglycerides	177.4*	200.4†
Normal (<200)	447	74.5
Borderline high (200–399)	131	21.8
Verv high (>1000)	9	2.2
Family history of IHD		
Yes	287	47.8
No	293	48.8
Don't know	20	3.3
Current smoking status		
Never smoked	388	64.7
Regular cigarette smoker	54 130	9.0 21.7
Occasional cigarette smoker	20	3.3
Pipe or cigar smoker	7	1.2
Not stated/refused	1	0.2
Sedentary lifestyle	101	=1.0
res	431 169	/1.8 28.2
* * *	105	20.2

+ Standard deviation.

 \pm Impaired glucose tolerance is defined as two-hour glucose levels of 140 to 199 mg/dL (7.8 to 11.0 mmol/L) on the 75-g oral glucose tolerance test.²⁷

CAD=coronary artery disease.

In this cross-sectional study of upper class Pakistanis, age, diabetes, and positive family history of IHD [ischemic heart disease] were strongly associated with CAD.

al design, and further research is required to study the association of diabetes, insulin resistance, and CAD in native Pakistanis.

Positive family history of IHD was also higher in the CAD group (Tables 4 and 5). Several studies have shown that though CAD is high in South Asians, conventional risk factors such as high blood pressure, high serum total cholesterol level, cigarette smoking, high-fat diet, and obesity consistently fail to fully explain these high rates.29 We found that rates of smoking, regular exercise, and hypertension did not differ between the two groups on multivariate analysis (Table 4). The rate of smoking is possibly an underestimation for several reasons. First, as seen in other developing countries like India,5,8,28 tobacco is consumed in, cheaper forms, like beedi (tobacco leaves rolled in a cigarette-like shape and wrapped with thread), hookah (tobacco mixed with molasses, burned, and smoked in a water pipe), chatha (crude tobacco leaves rolled in jackfruit leaves and smoked with the burning end inside mouth), and chewable forms. Our study considered only current cigarette smoking, assuming this to be a predominant form of tobacco consumption in higher socioeconomic classes. Second, we did not consider former smokers in the analysis, and third, women may under-report smoking. Since Pakistan is Islamic country, smoking in women is not freely discussed because of cultural and religious stigma. We found three of the 129 women ad-

	Coronary Arter	y Disease (CAD)		
Variable	Negative	Positive	OR (95% CI)*	P Value
Age	n %	n %		
<40 years	155 (32.0%)	11 (9.6%)		
\geq 40 years	330 (68.0%)	104 (24.0%)	4.4 (2.32, 8.5)	<.001
Gender				
Female	107 (22.1%)	22 (19.1%)		
Male	378 (77.9%)	93 (80.9%)	0.8 (0.5, 1.39)	.492
Menopause				
No	59 (55.1%)	5 (22.7%)		
Yes	48 (44.9%)	17 (77.3%)	4.2 (1.44, 12.15)	.009
BMI categories				
<25	151 (31.2%)	27 (23.5%)		
25-29.9	223 (46.1%)	66 (57.4%)	1.7 (1.01, 2.71)	.045
≥30	110 (22.7%)	22 (19.1%)	1.1 (0.61, 2.07)	.721
Diabetes				
No	416 (85.8%)	86 (17.1%)		
Yes	69 (14.2%)	29 (25.2%)	2.03 (1.24, 3.33)	.005
Hypertension				
No	392 (80.8%)	87 (75.7%)		
Yes	93 (19.2%)	28 (24.3%)	1.4 (0.84, 2.197)	.215
Cholesterol				
<200 mg/dL	345 (71.1%)	70 (60.9%)		
≥200 mg/dL	140 (28.9%)	45 (39.1%)	1.6 (1.04, 2.42)	.033
LDL				
<100 mg/dL	85 (75%)	20 (17.4%)		
>100 mg/dL	388 (79.7%)	95 (82.6%)	1.1 (0.73, 1.65)	.06
HDL				
<40 mg/dL	273 (91%)	67 (58.2%)		
≥40 mg/dL	212 (70.6%)	48 (41.7%)	1.5 (0.80, 1.73)	.030
Family history				
No	249 (53.1%)	44 (39.6%)		
Yes	220 (46.9%)	67 (60.4%)	1.7 (1.13, 2.63)	.011
Regular exercise				
Yes	132 (27.2%)	37 (32.2%)		
No	353 (72.8%)	78 (67.8%)	0.8 (0.51, 1.22)	.289
Regular smoking				
No	378 (78.8%)	84 (75.0%)		
Yes	102 (21.3%)	28 (21.5%)	1.2 (0.76, 1.997)	.389

Table 4. Univariate analyses on study subjects (N=600): dependent variable CAD vs non-CAD

mitting to being current cigarette smokers. Similar limitations were also observed in the NHSP report.¹⁷

Univariate analysis showed that general adiposity (BMI) and high cholesterol (\geq 200mg/dL) were significantly related to CAD. Body mass index (BMI) (25–29.9) and high cholesterol were independently and significantly as-

sociated with CAD, but in multivariate analysis the association was not significant (Table 4 and 5). This finding could be related to small sample size and convenience sampling method, which suggests that more aggressive identification and modulation of all known risk factors is needed, along with further epidemiologic studies, in this population. However, high triglyceride level was seen in few patients, which could be because of low consumption of alcohol because of religious obligations.

In addition, menopause in females was strongly associated with and independently related to CAD (OR 4.2, 95% CI 1.4–12.1) in univariate analysis (Table 4), and these results are similar to those seen in other studies.^{31,32} However, further detailed analysis on menopause was not performed because of small sample size.

LIMITATIONS

The study used the convenience sampling method, focused primarily on a high socioeconomic group visiting a teaching hospital for general preventive checkup. Most women do not visit hospitals for general checkups, which resulted in gender bias, and we were not able to analyze data according to gender. But keeping in mind the lack of research in Pakistan on increasing CAD and its risk factors, this study indicates a need for further work in Pakistan at a national level. Most Pakistanis belong to a low socioeconomic group; however, because the high socioeconomic class is considered to be a high-risk group for CAD, we focused on these early adopters, which are increasing in number because of improvements in the economy.

CONCLUSION AND RECOMMENDATIONS

This study is the first of its kind evaluating CAD risk factors and behaviors in the rising high socioeconomic group of Pakistanis, as this group undergoes epidemiologic transition. We could not find an association between CAD and some of the risk factors, like smoking and hypertension, which are modifiable and independently significantly related to CAD in previous studies. Furthermore, prospective studies will explain the major variations seen in

	Coronary Arter	y Disease (CAD)		
Variable	Negative	Positive	OR (95% CI)	P Value
Age				
<40 years	155 (32.0%)	11 (9.6%)		
\geq 40 years	330 (68.0%)	104 (24.0%)	4.04 (2.09, 7.8)	<.001
Diabetes				
No	416 (85.8%)	86 (17.1%)		
Yes	69 (14.2%)	29 (25.2%)	1.7 (0.99, 2.87)	.051
Family history				
No	249 (53.1%)	44 (39.6%)		
Yes	220 (46.9%)	67 (60.4%)	1.8 (1.17, 2.78)	.008

Table 5.	Multiple	logistic	regression	on study	subjects	(N=600)
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the nature of risk variables associated with CAD in the Pakistani population.

Given the strong association of major risk factors with CAD, understanding the unique characteristics of South Asians with CAD risk factors is important. Public health efforts should be focused on increasing the awareness of CAD and its determinants, with special emphasis on the high-risk group.

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AUTHOR CONTRIBUTIONS

Design and concept of study: Dodani Acquisition of data: Dodani Data analysis and interpretation: Dodani Manuscript draft: Dodani Statistical expertise: Dodani Acquisition of funding: Dodani Administrative, technical, or material assistance: Dodani