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Research article

Cardiometabolic risk factors associated with coronary artery disease in Asian Indian population

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Abstract

Coronary artery disease (CAD) has become a leading cause of mortality in both developed and developing countries. The present study was intended to explore the metabolic risk factors associated with high prevalence of CAD in Asian Indians. We recruited 1375 human subjects (660 angiographically confirmed CAD patients and 715 healthy controls) aged 25-85 years from north India. Standard anthropometric, socioeconomic and quantitative measurements were done in all the participants. Alcohol consumption and smoking emerged as a major risk factor for developing CAD (Odd ratio; 2.9 (2.22-3.89) p≤0.000 and 5.2 (3.34-8.09) p=0.000) respectively. The physical activity was significantly lower in CAD patients than controls. CAD patients had marked abdominal adiposity as reflected by their significantly higher Waist to Hip Ratio (WHR) and waist circumference. Also significantly higher body fat (%) was observed in women CAD patients (43.8±5.9) than their male counterparts (26.9±6.1). The reduced HDL-cholesterol and elevated creatinine values observed in CAD patients may have contributed to the pathophysiology of CAD and renal dysfunctioning in this study. The atherogenic indices i.e. TC/HDL ratio and the LDL/HDL ratios significantly predicted the primary cardiovascular risk in control subjects. In conclusion, the present study established low socioeconomic status, unhealthy diet and sedentary lifestyle, abdominal obesity, high alcohol consumption and smoking and dyslipidemia emerged as the metabolic risk factors contributing to the pathophysiology of CAD in Asian Indians. Large studies are necessary to determine the genetic predisposition in the pathogenesis of CAD in this population.

Key words: Cardiovascular disease, central adiposity, dyslipidemia, metabolic risk factors.

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1. Introduction

Cardiovascular diseases (CVD) have become a crucial social health problem in India and other developing countries [1, 2]. The facts show that these diseases are flourishing in these countries as compare to developed nations of Europe and North America [3, 4]. Coronary artery disease (CAD) being the major killer in developed countries is now promptly thriving in developing countries [5]. The South Asian Countries share most of the burden of cardiovascular diseases in comparison with any other region globally [6-8]. Recent estimates predicts that cardiovascular diseases will be the greatest cause of death and disability in India by 2020 [9]. Various studies have had suggested that age is a significant factor to which the risk factors of CVD are linked [10-12]. The cardiovascular risk for men and women, is known to escalate with age, smoking, hypertension, blood lipids and glucose levels, and central obesity [13]. The fact remains that the problems of high blood pressure and obesity, considered to be the major risk factors for CVD, are increasingly assuming global importance [14]. The major established cardiovascular risk factors include hypertension, smoking, hypercholesterolemia and type 2 diabetes mellitus [15, 16]. The majority of patients who develop CAD have at least one of these risk factors. The risk factors related to urban lifestyle such as unhealthy diet and sedentary lifestyle complement insulin resistance further ensuing cardiovascular risk. Many studies have been carried out in south Indians but data on north Indian population is scanty. So, this study was planned to determine the metabolic risk factors associated with the high prevalence of CAD in Asian Indian population.

2. Materials and Methods

Human subjects

The present study was commenced in year 2011 with the objective of identification of genetic and environmental risk factors associated with CAD in North Indian population. The study was verbally explained to all the participants and adequate opportunities were given for discussion with the interviewer. Informed written consent was then obtained from all the study subjects. All the protocols were approved by Institutional Ethics Committees of Panjab University, Chandigarh and Post Graduate Institute of Medical Education and Research, Chandigarh, India.

In this study, we included 1375 participants, among which 715 subjects were healthy controls and 660 subjects were angiographically confirmed CAD patients recruited from OPD of Advanced Cardiac Centre, PGIMER, Chandigarh. Potential participants identified were invited to participate in this study. After confirming eligibility, a full clinical examination was performed on each participant. The diagnosis of the occurrence of CAD was performed by cardiologist based on the clinical symptoms, characteristic ECG changes, cardiac enzyme levels, and the findings in coronary angiography and/or echocardiography. Other health conditions were documented based on self-reported history of diabetes, hypertension and related complications. Family history for all of the above conditions was also obtained. A detailed questionnaire was administered to each participant regarding their demographic and socioeconomic characteristics like participant's self-reported age, sex, educational status, family history and individual's smoking and alcohol use.

Inclusion/ Exclusion criteria

Individuals aged 25 years and above, irrespective of disease status were included in this study. Participants belonging to north Indian states only were included in this study.

Anthropometric measurements

Standard anthropometric measurements were performed including height, weight, waist and hip circumferences and blood pressure. Waist and Hip circumference was measured with a metal tape using standard protocols. Height was measured with a stature meter and weight with a portable balance beam scale. Blood pressure was measured by Omron blood pressure machine in sitting position from the left arm resting on the table, with legs uncrossed and feet flat.

Biochemical estimations

About 5 ml of blood sample of each patient was drawn in plain and EDTA coated vials. Quantitative lipid profile [total cholesterol (TC), triglycerides (TG), high density lipoprotein (HDL), and creatinine content were measured in serum by using standard kits (Roche Diagnostics, GmbH, Mannheim, Germany). Low-density lipoprotein (LDL) level was calculated by using Friedewald formula i.e. LDL-C = TC – [HDL-C – (TG in mg/dl/5)]. Fasting and random blood glucose levels were measured using a portable glucometer (Abbott OptiumXceed, USA). Calibration of the glucometer was routinely verified using test strips provided by the manufacturers. All the quantitative parameters were measured by following manufacturer's instructions using biochemistry autoanalyzer.

Quantitative measures of obesity

Body Mass Index (BMI) was calculated according to Quetelet equation i.e. (BMI = weight in kilograms/height in meters squared). Waist to Hip Ratio (WHR) was calculated as ratio of abdomen to hip circumferences. Anthropometric measurements used for the establishment of abdominal obesity were according to the cut off values for Asian Indians. Body fat percentage (BF %) was calculated according to the method of Lean et al. [17] using following formulae; BF% for men = [(0.567 × waist circumference in cm) + (0.101 × age in years)] − 31.8; and BF% for women = [(0.438 × waist circumference in cm) + (0.221 × age in years)] − 9.4.

Phenotypic characteristics

The abdominal obesity was measured according to the new cut offs proposed for South Asian Indians [18] i.e. WHR >0.89 for men and > 0.81 for women. BMI <23 kg/m^2 has been proposed for low risk, 23-27.5 kg/m^2 for increased risk and ≥27.5 kg/m2 for high risk for developing weight- related diseases in Asian populations. Dyslipidemia is the elevation of cholesterol (>200mg/dl), triglycerides (>150mg/dl) or both, or a low HDL level (<40 mg/dl in men and <50 mg/dl in women)that contributes to the development of atherosclerosis. Hypertension was defined as a persistent elevation of blood pressure ≥140/≥90 mmHg or use of any antihypertensive medication.

Statistical Analysis

Results were expressed as mean ± SD. Chi-square analysis was applied to test the significance of differences in frequencies. Group comparisons were done using unpaired t-tests. All the p-values <0.05 (two-tailed) were considered as significant difference. Logistic regression analysis were performed to correlate various clinical parameters with disease and to calculate odds ratios (ORs) and 95% CIs for each risk factor. Statistical

analysis was performed using IBM-SPSS for Windows, version 20 (SPSS, Inc., Chicago, IL).

3. Result and Discussion

Among 1375 participants, 715 subjects were healthy controls (307 Men and 408 Women) and 660 subjects were CAD patients (525 Men and 135 Women). During this study, 166 subjects were diagnosed with CAD after their first visit to the hospital as they were showing symptoms of CAD earlier. The disease status of all these newly diagnosed CAD patients was confirmed after undergoing angiography procedures. The demographic and socioeconomic characteristics of study participants are summarized in Table 1. Most of the participants originated from Chandigarh followed by Punjab, Haryana, Himachal and other parts of North India and belonged to Hindu (51.9%) and Sikh communities (46%). Only 2% belong to Muslim and Christian communities. A significant difference was observed between CAD patients and control subjects in respect of socio-economic status and eating habits. Alcohol consumption was significantly higher in CAD patients and may increase the risk of CAD in this population (OR, with 95% CI; 2.9 (2.22-3.89) P=0.000). The physical activity was significantly lower in CAD patients than controls. Due to religious belief, Sikhs and most of the Indian women don't smoke.

Table 1. Demographic and socioeconomic characteristics of the study participants

Characteristics		Control	CAD patients	Total	p value
Educational qualifications	Illiterate	30 (4.2%)	112 (17%)	142 (10.3%)	0.000
	Primary	127 (17.8%)	332 (50.3%)	459 (33.4%)	
	Higher secondary	151 (21.1%)	55 (8.3%)	206 (15%)	
	Technical diploma	20 (2.8%)	22 (3.3%)	42 (3.1%)	
	University degree	387 (54.1%)	139 (21.1%)	526 (38.3%)	
Socioeconomic status	High Income class	51 (7.1%)	27 (4.1%)	78 (5.7%)	0.510
	Middle class	530 (74.1%)	503 (76.2%)	1033 (75.1%)	
	Low income class	134 (18.7%)	130 (19.7%)	264 (19.2%)	
Cooking media	Refined oil	152 (21.3%)	215 (33%)	367 (26.8%)	0.000
	Hydrogenated oil	71 (9.9%)	21 (3.2%)	92 (6.7%)	
	Mustard oil	103 (14.4%)	219 (33.6%)	322 (23.6%)	
	Clarified butter	17 (2.4%)	18 (2.8%)	35 (2.6%)	
	Olive oil	10 (1.4%)	10 (1.5%)	20 (1.5%)	
	Mixed oil	362 (50.6%)	169 (25.9%)	531 (38.8%)	
Eating habits	Vegetarian	30 (63.8%)	362 (61%)	392 (61.3%)	0.416
	Non vegetarian	17 (36.2%)	231 (39%)	248 (38.8%)	
Smoking	Non smokers	685 (95.8%)	474 (71.8%)	1159 (84.3%)	0.000
	Active smokers	29 (4.1%)	151 (22.9%)	180 (13.1%)	
	Left smoking	1 (0.1%)	35 (5.3%)	36 (2.6%)	
Alcohol consumption	Teetotaller	623 (87.1%)	440 (66.7%)	1063 (77.3%)	0.000
	Drinkers	89 (12.4%)	185 (28%)	274 (19.9%)	
	Left drinking	3 (0.4%)	35 (5.3%)	38 (2.8%)	
Physical Activity	Very Active	143 (20%)	68 (10.3%)	211 (15.3%)	0.000
	Moderately Active	520 (72.7%)	559 (84.7%)	1079 (78.5%)	
	Sedentary life style	52 (7.3%)	33 (5%)	85 (6.2%)	

However, smoking emerged as a major risk factor for developing CAD in this population (OR, with 95% CI; 5.2 (3.34-8.09) p=0.000). Unlike Western populations, the frequency of non-vegetarian diet among all the participants (38.8%), in general, was very low (once a week or once a month) with the exception of <3.1% of individuals who were regularly following a non-vegetarian diet. Also, consumption of hydrogenated oil (trans fat) and mixed oils used in daily cooking may increase the risk of CAD many folds in our study (OR, with 95% CI; 4.782 (2.817-8.119), p=0.000 and 3.03 (2.298-3.995, p=0.000), respectively.

Age specific prevalence of CAD is shown in the Figure 1. Present data demonstrated that prevalence of CAD increased with age especially after 55 years and has the strongest age associated risk for CAD among Asian Indians. One-third CAD patients developed this disease at a mean age of 58 years having the duration of 1-6 months.

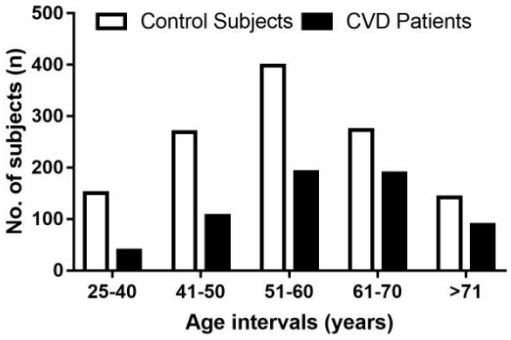


Figure 1. Age specific prevalence of CAD in Asian Indians

The maximum number of CAD patients were in the age range of 51-70 years. Logistic regression analysis of the data established that our population has the strongest age associated risk for developing CAD in the age interval of 55-65 years (OR with 95% CI is 5.387 (3.821-7.594); p=0.000) and >65 years age group (OR; 8.101 (5.417-12.11); P=0.000).

Table 2 shows the anthropometric measurements in the study subjects. A significance difference in the mean age of the CAD patients (58.6±11.2 years) and healthy controls (49.5±10.8 years) was observed (p=0.000). Most of the CAD patients develop this condition in the most productive years of their life which is 10-15 years earlier and remain undiagnosed for many years. A majority of the CAD patients were suffering from hypertension and were taking anti-hypertensive drugs to limit their blood pressure levels to normal.

Abdominal obesity reflected by higher waist circumference was predicted as one of the major risk factor for the development of CAD in our study (Figure 2). Pragmatically, the control subjects were found to be at a high risk of developing metabolic disorders, due to their significantly higher BMI as compared to CAD patients (Table 2).

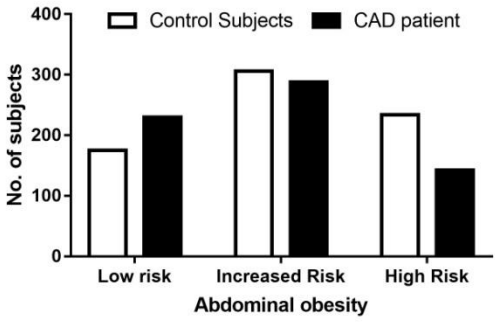


Figure 2. Prevalence of abdominal Obesity in Asian Indians

However, CAD patients had marked abdominal adiposity as reflected by their significantly higher WHR when compared with control subjects. Following stratification of the data, taking BMI cutoffs into account by WHO Expert Consultation, 2004, we observed pronounced central obesity in both CAD patients and controls (Figure 3), even at the lowest BMI values (<23kg/m^2). Present study demonstrated that 68.8% of controls and 64.8% of CAD patients fall under the higher limits of waist

Table 2. Anthropometric Characteristics of study participants stratified by sex and disease status in Asian Indians

Parameters	Disease status	Male subject				Female subjects				Total subjects			
		N	Mean	SD	p	N	Mean	SD	p	N	Mean	SD	p
Age(years)	Control	307	50.7	11.5	0.000	408	48.6	10.1	0.000	715	49.5	10.8	0.000
	CAD Patient	525	58.7	10.9		135	58.2	12.2		660	58.6	11.2	
WC (inches)	Control	307	36.91	6.77	0.486	408	34.98	4.48	0.004	715	35.81	5.66	0.005
	CAD Patient	525	36.65	4.16		135	36.27	4.45		660	36.57	4.22	
HC (inches)	Control	307	38.77	6.93	0.000	408	39.37	4.20	0.001	715	39.11	5.54	0.000
	CAD Patient	525	37.21	3.92		135	37.92	4.25		660	37.36	4.00	
SBP (mm Hg)	Control	307	134	19	0.871	408	128	19	0.003	715	130	19	0.004
	CAD Patient	525	133	20		135	134	22		660	133	20	
DBP (mm Hg)	Control	307	83	10	0.709	408	80	10	0.009	715	81	10	0.001
	CAD Patient	525	83	11		135	83	14		660	83	12	
WHR	Control	307	0.95	0.059	0.000	408	0.89	0.081	0.000	715	0.92	0.079	0.000
	CAD Patient	525	0.99	0.048		135	0.96	0.068		660	0.98	0.054	
BMI (kg/m^2)	Control	307	24.98	4.46	0.070	408	26.62	4.49	0.000	715	25.92	4.55	0.000
	CAD Patient	525	24.45	3.80		135	24.91	4.66		660	24.54	3.99	
Body fat (%)	Control	307	26.47	9.79	0.436	408	40.25	5.59	0.000	715	34.33	10.27	0.000
	CAD Patient	525	26.90	6.06		135	43.82	5.94		660	30.36	9.11	

WC, Waist Circumference; HC, Hip Circumference; SBP, Systolic Blood Pressure; DBP, Diastolic Blood Pressure; WHR, Waist to Hip ratio; BMI, Body Mass Index

circumference recommended for Asian Indians, reflecting a strong predisposition to cardiometabolic abnormalities in our population. Body fat percent was significantly higher in control subjects than CAD patients (p=0.000). Also significantly higher body fat was observed in women CAD patients (43.8±5.9) than their male counterparts (26.9±6.1).

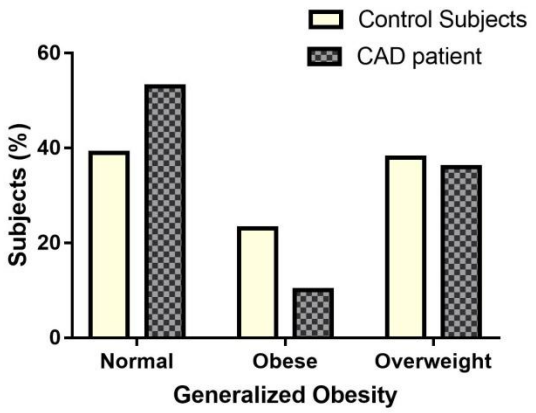


Figure 3. Prevalence of Generalized Obesity in Asian Indians

Table 3 shows the clinical characteristics in the CAD patients and healthy control subjects. The mean glucose level was significantly higher in CAD patients than in control subjects. The influence of dyslipidemia in the progression of CAD is well established. Our study demonstrated significantly higher levels of TC, TG, LDL and VLDL in control subjects than CAD patients, the reason being most of the CAD patients were taking lipid lowering drugs. Also CAD patients are very regular in taking prescribed medicines along with daily exercises/sports. Present data also revealed that the males have slightly higher HDL level than normal but all female subjects were having below normal value of HDL-cholesterol. The reduced HDL-cholesterol and elevated creatinine values observed in CAD patients may have contributed to the pathophysiology of CAD and renal dysfunctioning in this study. In an attempt to optimize the predictive capacity of the lipid profile, atherogenic indices have been defined. The TC/HDL ratio and the LDL/HDL cholesterol ratio are two important components and indicators of vascular risk, the predictive value of which is greater than the isolated parameters. These ratios can provide information on risk factors difficult to quantify by routine analysis and could be a better representation of the metabolic and clinical interactions between lipid fractions. In the control subjects, 33.2% and 26.9% individuals have significantly greater primary cardiovascular risk as demonstrated by atherogenic indices i.e. TC/HDL and LDL/HDL ratios owing to the imbalance between the cholesterol carried by atherogenic and protective lipoproteins.

Discussion

There has been an alarming increase in the prevalence of cardiovascular mortality in India and other south Asian countries [19-21]. CVD is a multifactorial disease in which both environmental and genetic factors interplay [22]. In the present study, we have identified various cardiometabolic risk factors such as low SES, smoking, alcohol consumption, low physical activity alongwith bad combination of cooking media, which are associated with high prevalence to CVD in Indian population. Our results are inconsistent with other studies carried out in Asian Indians [19-21, 23, 24]. Indian economy growing at a rapid pace has induced inequities in education, incomes and socioeconomic status [25], resulting poor health status [26]. In addition, a reversal of socio-economic gradients for CAD risk factors has emerged in the Indian population [27, 28]. In developed countries where the epidemic has been there for many decades, high incidence of CAD first occurred in high socio-economic group followed by a reversal of the trend. Studies in India over the past half century have

Table 3. Biochemical measurements in the study subjects stratified by sex and disease status in Asian Indians

Parameters	Disease status	Male subject			Female subjects			Total subjects		
		Mean	SD	p	Mean	SD	p	Mean	SD	p
Glucose (mg/dl)	Control	92.44	11.57	0.000	92.44	10.72	0.000	92.44	11.07	0.000
	CAD Patient	100.28	15.18		97.52	13.47		99.67	14.85	
TC (mg/dl)	Control	188.69	45.66	0.000	195.89	42.96	0.000	192.83	44.24	0.000
	CAD Patient	151.34	43.37		162.68	47.45		153.79	44.48	
TG (mg/dl)	Control	164.60	81.67	0.005	145.22	62.28	0.542	153.46	71.76	0.107
	CAD Patient	148.59	66.53		141.26	54.36		147.00	64.11	
HDL(mg/dl)	Control	45.30	7.18	0.000	46.17	8.22	0.039	45.80	7.80	0.000
	CAD Patient	42.90	5.96		44.37	7.93		43.22	6.46	
LDL(mg/dl)	Control	110.47	42.89	0.000	120.68	41.91	0.000	116.34	42.60	0.000
	CAD Patient	78.72	41.77		90.06	42.87		81.17	42.23	
VLDL(mg/dl)	Control	32.92	16.33	0.005	29.04	12.46	0.542	30.69	14.35	0.107
	CAD Patient	29.72	13.31		28.25	10.87		29.40	12.82	
Total Lipids (mg/dl)	Control	545.51	156.05	0.000	537.00	121.01	0.000	540.62	136.96	0.000
	CAD Patient	451.26	123.03		466.63	132.10		454.59	125.08	
TC/HDL ratio	Control	4.28	1.31	0.000	4.37	1.24	0.000	4.33	1.27	0.000
	CAD Patient	3.60	1.19		3.79	1.47		3.64	1.26	
LDL/HDL ratio	Control	2.49	1.18	0.000	2.72	1.13	0.000	2.62	1.16	0.000
	CAD Patient	1.88	1.06		2.12	1.23		1.93	1.10	
Creatinine (mg/dl)	Control	0.95	1.05	0.102	0.75	0.41	0.001	0.83	0.76	0.000
	CAD Patient	1.09	0.91		0.90	0.37		1.04	0.81	

TC, Total Cholesterol; TG, Triglycerides; HDL, High Density Lipoprotein; LDL, Low Density Lipoprotein; VLDL, Very Low Density Lipoprotein

revealed a similar trend towards a progressive reversal of the social gradient for CAD. The prevalence of CAD has also risen substantially in India [29, 30] and was reported to be higher in urban than in rural areas [31]. Our study showed that alcohol consumption and smoking increased the risk of developing CAD among study population. Smoking was also shown to predispose to CAD through a variety of mechanisms [32]. Our findings that high- and middle-income groups had a significant risk of having CAD are consistent with the previous studies done in north India [33]. Highly educated persons and those belonging to the most affluent class had significantly greater consumption of calories, polyunsaturated fats, fruits, vegetables and fibers as compared to the most deprived men and women.

Our study demonstrated the enhanced risk of CAD with use of hydrogenated oil and mixed oils on daily basis. Amongst Asian Indian vegetarians, the lipoprotein levels are not different from non-vegetarians [34, 35]. This trend is due to contaminated vegetarianism, where vegetarians consume profuse amounts of dairy, butter, ghee, cheese and bakery products, all of them are major sources of saturated fat and/or trans unsaturated fatty acid [34]. A research study signifies that a diet very low in fat and very high in carbohydrate can intensify dyslipidemia by increasing triglycerides and decreasing HDL levels [36].

Epidemiological studies from various parts of India have reported the rising trends and a high burden in the levels of conventional risk factors such as diabetes, hypertension and metabolic syndrome which are largely determined by urbanization as evident from the urban-rural difference in the risk factors observed in India [37-39]. The major established cardiovascular risk factors include hypertension, smoking, hypercholesterolemia and type 2 diabetes mellitus [16, 40]. Various explanations have been anticipated for this extreme vascular risk including variation in access to healthcare, risk factor burden and clustering and socioeconomic variables [41]. While the exact aetiology of this predisposition to CVD among Indians is still debated, rapid transition in diet and lifestyles with urbanization are identified as the major contributors to this epidemic [6]. Elevated blood pressure is a significant risk factor for the progression of CVD [42].

Some metabolic abnormalities were more prevalent among Asian Indians, including high triglyceride, type 2 diabetes mellitus, and central or visceral obesity [43, 44]. The present study demonstrated low physical activity, abdominal obesity and dyslipidemia as major cardiometabolic risk factors in predisposition of CAD among study subjects. The typical "Asian Indian phenotype" refers to a blend of clinical, biochemical and metabolic abnormalities that are more common in individuals of South Asian origin and thus tendency of this group for developing diabetes and premature CAD [45, 46]. Previous studies showed lower physical activity as a major risk among the CAD patients [23, 47, 48]. About 12% of the global burden of myocardial infarction is because of sedentary lifestyle [49]. The waist circumference, glucose and insulin levels, BMI, were inversely related with levels of physical activity in South Asians [50].

Various studies have quoted that age is the main factor to which the CVD risk factors are related [10]. CVD results in substantial number of deaths in working age group in India as it manifests here almost 10 year prior on an average than other countries in the world [51]. This demographic transition has brought most people to the age group where the CVDs perceive. Thus, a larger population of liable adults in India confers to the CVD inflicted population. Lower physical activity scores have been reported in South Asians compared with white

populations [50, 52, 53]. Levels of physical activity were inversely associated with BMI, waist circumference, glucose and insulin levels in South Asians [50]. The data showing physical activity suggested that those leading a sedentary lifestyle developed CAD and other metabolic diseases more frequently than those with an occupation or routine life involving more physical work. Consistently, South Asians and Asian Indians have been shown to be less physically active when compared with other ethnic groups [24].

Prevalence of overweight and obesity was highest in southern and northern Indian states and lowest in central Indian states [54]. Although possessing lower prevalence of obesity as defined by BMI, Asian Indians are predisposed to have greater waist circumference and waist-to-hip ratios, contributing to greater degree of central obesity. Our study depicted similar results with majority of the study subjects having greater waist circumference. Also, the BMI<25 was observed in the CAD patients. The traditional cut-off point of BMI of 25 might not define overweight and obesity optimally in Asian Indians as they have higher percentage of body fat compared to whites [55]. Among CAD patients, women tend to have significantly more body fat percent as compared to men. Asian Indians have more total abdominal and visceral fat for any given BMI, and for any given body fat they have increased insulin resistance [56, 57]. The higher incidence of CVD events in obese patients seems to be associated to endothelial dysfunction and subclinical inflammation in addition to the worsening of CVD risk factors [58]

Present finding concurs with an Indian study [59] which showed that only 8.2% of patients with angiographically proven CAD had a BMI >27 kg/m2 but contrasts with western studies which have shown a strong association of BMI with hyperglycaemia and dyslipidaemia [60, 61]. High BMI is associated with the development of cardiovascular (CV) risk factors such as hypertension, dyslipidemia, insulin resistance, and diabetes mellitus leading to cardiovascular diseases such as coronary heart disease (CHD) and ischemic stroke [62-64]. The development of these co morbidities is proportionate to the BMI and obesity is considered as an independent risk factor for CVD [65, 66]. Several studies have documented that a high BMI is significantly associated, in both men and women, with manifestations of CVD such as angina, myocardial infarction (MI), heart failure and sudden death [67, 68]. The higher incidence of CVD events in obese patients seems to be related to endothelial dysfunction and subclinical inflammation in addition to the worsening of CVD risk factors.[58] Despite having lower prevalence of obesity as defined by BMI, Asian Indians tend to have greater waist circumference and waist-to-hip ratios, thus having a greater degree of central obesity. Again, Asian Indians have more total abdominal and visceral fat for any given BMI, and for any given body fat they have increased insulin resistance [56, 57]. The body fat (%) is a measure of physical fitness. Women tend to have greater essential fat than men because of child bearing and hormonal functions. In our study, central obesity reflected by higher waist circumference and WHR may contribute a major cardiometabolic risk in Asian Indians. A study in 52 countries showed that more than 80% of the global burden of CAD could be attributed to these main established risk factors and to a lack of exercise [49].

Dyslipidemia is more prominent in Asian Indians and poses a major threat for the development of CAD in our population. Once diagnosed with CAD, regular use of lipid lowering drugs by CAD patients limits the lipid profile to near normal values. High LDL-C levels considered as bad cholesterol leads to the formation of plaque in the

artery, hence causing CAD. Previous studies showed that this LDL-particle phenotype represented an independent risk factor for CAD [69, 70]. Many studies have reported that Asians have higher prevalence of lipid abnormalities compared with non-Asians [71, 72]. Our study showed higher TC, TG and LDL-cholesterol among the control subjects when compared with CAD patients. The probable reason for this pattern may be the regular intake of lipid lowering drugs by CAD patients. Lipid lowering drugs such as statins inhibit 3-hydroxy-methylglutaryl coenzyme A (HMG-CoA) reductase enzyme which is responsible for the reduction in the serum low-density lipoprotein (LDL)-cholesterol level. The statins also have demonstrated efficacy in patients with a broad range of initial cholesterol levels but without coronary artery disease and in patients with average cholesterol levels and coronary artery disease. Intensive lipid-lowering therapy with statins not only improves survival rates and clinical outcomes but also reduces the progression of atherosclerosis [73-76]. The study also showed decreased HDL and increased creatinine levels among CAD patients. Low levels of HDL cholesterol have been shown to be a powerful risk factor for CAD [77]. Classic cardiovascular risk factors such as age, gender, smoking, type 2 diabetes, hypertension, high LDL and low HDL cholesterol levels have been widely established as independent cardiovascular risk factors [78]. Furthermore, the TC/HDL and LDL/HDL ratios are of great interest as major predictors of cardiovascular disease. Previous studies suggested TC/HDL ratio as a powerful coronary risk predictor than independently used total cholesterol, LDL cholesterol and HDL cholesterol [79, 80]

Insulin resistance was shown to increase the risk of both T2DM [81, 82] and CVD [83]. The increased prevalence of insulin resistance and T2DM in South Asians appears to be a major contributor to the observed elevated vascular risk. The hyperinsulinemia in these patients accelerates the atherosclerotic process in the coronary arteries. Hyperinsulinemia, insulin resistance, and the higher rate of prevalence of metabolic syndrome in people with type-2 diabetes were attributed to high coronary risk in south Asians [39, 84-89].

In conclusion, present study established the major cardiometabolic risk factors in north Indian population. We observed an early progression to CAD which, in part, is due to the physiologic attributes, such as upper-body adiposity as evident by a high WHR, body fat percent, physical inactivity, hypertension and low HDL-Cholesterol. Large studies need to be conducted to determine whether a genetic predisposition can be one of the contributing factors in the pathogenesis of CAD in this population.

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