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A STUDY OF RISK FACTORS FOR CORONARY ARTERY DISEASE IN A TERTIARY CARE HOSPITAL IN CENTRAL INDIA: A CASE-CONTROL STUDY

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Abstract

Background: Infectious and nutritional diseases are on the decline, while non-communicable diseases (NCDs) are becoming increasingly prevalent among adults, emerging as a significant cause of morbidity and mortality. The majority of NCD-related deaths are attributed to cardiovascular diseases (CVDs). Coronary artery disease (CAD) is a complex, multifactorial condition associated with various risk factors, both modifiable and non-modifiable, that may be generalized or systemic. However, many of the risk factors for CAD are modifiable and contribute substantially to the population's overall risk. **Methods:** A hospital-based case-control study was conducted involving newly diagnosed cases of coronary artery disease. The control group consisted of patients admitted to the same hospital for eye, ear, or nose conditions, or those admitted to the surgical ward for non-systemic diseases, excluding cancer and prostatic hypertrophy. Cases and controls were selected in a 1:1 ratio, comprising 130 cases and 130 controls. Matching for age and gender was performed. **Results:** The factors which were significantly associated with CAD in univariate analysis in decreasing order of strength of association were total cholesterol more than or equal to 200mg/dl, hypertension, tobacco smoking, family history of CAD, LDL cholesterol more than or equal to 130mg/dl, diabetes mellitus, physical activity less than 30min/d, and screen time more than 2h/d. On multiple logistic regression, among risk factors, the decreasing order of strength of association with CAD were tobacco smoking, hypertension, family history of CAD, and diabetes mellitus. **Conclusion:** Risk factors like tobacco smoking, hypertension, family history of CAD and diabetes mellitus were significantly associated with CAD.

Keywords: Coronary artery disease, Risk factors, Cardiovascular diseases

Introduction

There is a rapid epidemiological transition around globe. Infectious and nutritional diseases are decreasing, and non-communicable diseases (NCD) are increasing among adults making them as common cause of morbidity and mortality.[1] It is projected that by 2020, NCD's account for 73% deaths and 60% disease burden.[2] WHO predicts that by 2030, worldwide, 14.9% deaths in men and 13.1% deaths in women will be caused by coronary artery disease (CAD).[3] In terms of attributable deaths, the leading NCD risk factor globally is raised blood pressure (13%

worldwide deaths are attributed), followed by tobacco use (9%), raised blood glucose (6%), physical inactivity (6%) and overweight, obesity (5%).[4]

Most of NCD deaths are due to cardiovascular diseases (CVDs).[5] In 2016, out of total deaths, India reported, 63% were because of NCD's of which 27% were attributed to CVDs. CVDs include a group a disorder of heart and blood vessels and they include Coronary heart disease, Cerebrovascular disease, Rheumatic heart disease and other conditions.[6]

CAD is a multifactorial disease.[7] There are a number of modifiable and non-modifiable risk factors associated with CAD which may be generalized or systemic.[8] But many of risk factors for CAD are modifiable and account for majority of population's attributable risk.[9]

The non-modifiable risk factors for CAD are Age, Gender, Family history of CAD. The modifiable risk factors are comorbidities like Diabetes Mellitus (DM), Hypertension, and behavioural risk factors.[10] Age is one of the strongest factors related to CAD.[11] Also, it is more common in men than in women.[12] Although the incidence of CAD is lower in women than men, women have a higher mortality and worse prognosis after acute cardiovascular events.[13] CAD increases with age, but there is a sharper increase in women.[12] A family history of heart disease has been associated with the risk of CAD in several studies.[14] A positive family history of CVD modifies future risk of CVD. Siblings of patients have a 40% increased risk and offspring of parents have a 60-75% increased risk of CAD.[15] It is a major risk factor not only because of genetic inheritance but also because of shared lifestyles that increase susceptibility to CAD.[16] The most important behavioural risk factors are unhealthy diet, physical inactivity, tobacco use, and alcohol consumption.[17] Sedentariness among adults is associated with more risk of premature mortality, heart disease, obesity, and insulin resistance. Among all sedentary activities, the most popular is screen time (i.e watching television/ DVDs/videos/computer use.[17] The consequences of these behavioural risk factors may show up as raised blood pressure, raised blood glucose, raised blood lipids, overweight and obesity.[6] Another upcoming risk factor of CAD is mental stress. Chronic stress increases the risk of incident CAD while acute stress can trigger coronary heart disease events in vulnerable patients.[19] Mental stress induced myocardial infarction (MSIMI) is associated with a 3-fold higher rate of fatal cardiac events.[18] Among metabolic factors, high triglyceride concentration, low concentration of High-Density Lipoprotein (HDL) is associated with higher risk of ischemic heart disease (IHD) and are more prevalent among South Asians.[20,21]

CAD is common and it is preventable. The risk factors can be screened, identified and treated early even at primary care facilities. Secondary prevention is also an important task to improve prognosis of patients with CAD. The continuing surveillance of these risk factors as they are measurable and modifiable helps in planning of preventive activities in the control of NCDs.[22] There is a need to understand ways of healthy ageing as we live in a society with rising life expectancy.[7] To support this, WHO "Global Action Plan for prevention and control of NCDs 2013-2020" aims to reduce the number of premature deaths from NCDs by 25% by 2025.[6] Considering the rising burden of CAD in India and as most of the risk factors are modifiable, this study was conducted to determine the distribution and association of some risk factors with CAD.

Materials and Methods

A hospital-based case-control study was conducted at a tertiary care hospital over the course of one year, from November 2020 to October 2021, following approval from the institutional

ethics committee. The study focused on newly diagnosed cases of Coronary Artery Disease (CAD), identified by a physician based on typical symptoms such as retrosternal pain, breathlessness, and sweating, and confirmed through ECG. Patients with heart diseases other than CAD, including congenital heart disease, valvular heart disease, cor pulmonale, as well as those with a history of CAD, cerebrovascular episodes, or other conditions like renal disease, liver cirrhosis, and COPD, were excluded from the study.

The control group consisted of patients admitted to the same hospital for conditions related to the eye, ear, or nose, or those in the surgical ward not admitted for systemic diseases, cancer, or prostatic hypertrophy. To ensure the validity of the control group, a history of CAD was taken, confirming that the controls had never been admitted for CAD or received treatment for the condition. Matching was done for age and gender between cases and controls. Several risk factors were assessed in the study, including diabetes mellitus, hypertension, physical inactivity, diet type, tobacco smoking, smokeless tobacco use, alcohol consumption, family history of coronary artery disease, sleep duration, screen time, mental stress, obesity, central obesity (assessed by waist circumference and waist-hip ratio), and dyslipidemia.

The sample size for the study was determined based on a previous study titled "Risk factors for Acute Myocardial Infarction in Coastal region of India: A Case-Control study" by Vinay Rao et al.,[23] which identified the proportion of hypertension among CAD cases as 0.52 and among controls as 0.22. Hypertensive individuals were found to have twice the risk of developing CAD compared to non-hypertensives. The required sample size was calculated using these proportions, with a significance level of 5%, a power of 80%, and standard values for normal deviates. This resulted in a sample size of 127 cases and 127 controls. However, the study ultimately included 130 cases and 130 controls.

Data collection involved enrolling the first three patients admitted with CAD in the medicine ward as cases on the day of data collection. All newly diagnosed cases meeting the inclusion criteria were included in the study until the sample size was reached. Control patients were selected from the ENT, ophthalmology, and surgery wards based on the predetermined criteria. The data collection proforma included sociodemographic characteristics such as age, gender, place of residence, occupation, socioeconomic status, history of present illness, and risk factors under study. Screen time was assessed by the duration of daily screen exposure, and stress was evaluated based on the number of life events in the past year using the Presumptive Stressful Life Events Scale (PSLES).[24]

Following the interview, a clinical examination was conducted, which included anthropometric measurements like height, weight, body mass index (using the South East Asian classification), waist circumference, hip circumference, and waist-hip ratio. General examinations recorded pulse rate, respiratory rate, and blood pressure, while systemic examinations covered the cardiovascular, respiratory, abdominal, and central nervous systems. Investigations such as fasting blood sugar and lipid profile measurements (including total serum cholesterol, triglycerides, low-density lipoprotein, and high-density lipoprotein) were also recorded.

For statistical analysis, the collected data was entered into Microsoft Excel and analysed using SPSS 20. Quantitative variables were expressed as mean and standard deviation, while categorical variables were expressed as percentages. The chi-square test and Yates corrected chi-square test were used to assess the association between exposure rates of cases and controls. A p-value of less than 0.05 was considered significant. The strength of the association between each risk factor and CAD was evaluated using the odds ratio.

Results

This hospital-based case-control study was conducted at a tertiary care hospital in Central India. The study included a total of 130 cases and 130 controls, maintaining a 1:1 ratio between the two groups. The mean age of the cases was 55.32 years with a standard deviation of 10.61, ranging from 34 to 87 years. In comparison, the mean age of the controls was 54.32 years with a standard deviation of 10.23, ranging from 36 to 85 years. The mean ages of the cases and controls were comparable. The study population consisted of 97 males (74.62%) and 33 females (25.38%) in both the case and control groups.

The analysis of age distribution revealed that among male participants, the majority (34.02%) were in the 51–60-year age group, while among female participants, the majority (36.37%) were in the 61–70-year age group. Significant risk factors associated with coronary artery disease (CAD) identified in the study included diabetes mellitus, hypertension, tobacco smoking, physical inactivity, and screen time.

Further analysis of the lipid profiles revealed that elevated levels of total cholesterol, triglycerides, and LDL cholesterol were significantly associated with CAD. Univariate analysis, conducted at a significance level of 5% (α=0.05) and a power of 20% (β=20%), identified several factors significantly associated with CAD. In decreasing order of the strength of association, these factors included total cholesterol levels of 200 mg/dl or higher, hypertension, tobacco smoking, a family history of CAD, LDL cholesterol levels of 130 mg/dl or higher, diabetes mellitus, physical activity of less than 30 minutes per day, and screen time exceeding 2 hours per day.

The study also ranked the risk factors for CAD in decreasing order of their strength of association. Tobacco smoking was identified as the strongest risk factor, followed by hypertension, a family history of CAD, and diabetes mellitus.

Discussion

This is a hospital-based case control study conducted in a tertiary care hospital in Central India with objectives to study distribution and association of some risk factors with coronary artery disease. In this study, the majority of the study participants were in the age group of 51-60 years. The mean age of cases was 55.32±10.61 and mean age of controls was 54.32±10.23. These findings were almost similar to the study conducted by Agrawal et al.[25] (2020) in which they found the mean age in CAD case and control group was 57.86±10.112 and 57.19±10.71, respectively. In a similar study done by Kaur et al.[26] (2016) found in their study that there was strong age associated risk for developing CAD in the age group of 55-65 years (OR=5.387, (95%CI=3.821,7.594), p=0.000). There were 97 males (74.62%) and 33 females (25.38%) in both cases and controls in our study. These results were similar to a study conducted by Sriharibabu et al.[27] (2012) found that there were 65.7% males and 34.3% females among CHD cases. Contrary results were seen in a study done by Gheisari et al.[28] (2020) in their study found that ischemic heart disease (IHD) was significantly higher in men compared to women (19.1% of 314 males versus 14.2% of 698 females) (p=0.04).

In this study, it was found that those who were having diabetes mellitus were at a higher risk of developing CAD compared to those who were not having diabetes mellitus and this association was found to be statistically significant (OR=2.53; 95%CI:1.52,4.19;

p=0.0002).Similar results were seen with a study conducted by Kapoor et al.[29] (2013) it was found that there was a significant association between diabetes mellitus and coronary artery disease [OR =4.5 (95% CI: 2.4-8.7) p<0.0001] and also in Vinay et al.[23] (2019) found a significant association between diabetes mellitus and coronary artery disease in their study (OR =1.9; 95%CI: 1.3-2.7).

Hypertension was found to be a significant risk factor for developing CAD (OR=3.33; 95%CI:2.00,5.54; p=0.0002) in our study. These findings were consistent with the study done by Kazemi et al.[30] (2011) who found that the odd of developing CAD is 3.2 times more in hypertensives compared to non-hypertensives. Hypertension was found to be a significant risk factor for CAD in a study conducted by Panchbhai et al.[31] (2018) (OR=36; p=0.0001).

In this study, it was found that those who had a family history of CAD are at a higher risk for developing CAD and it is statistically significant (OR=2.76; 95%CI:1.56,4.86; p=0.0003). A study conducted by Gupta et al.[32] (2016) found a significant association between family history of CAD and CAD (p<0.05) and also a similar study conducted by Sharma et al.[33] (2017) it was found that there was a significant association between family history of CAD and CAD [OR=5.0; 95%CI:1.7,4.8; p<0.002].

In this study, it was found that 65(50.00%) were smokers among cases and 30 (23.08%) were smokers among controls. It was found that tobacco smoking was a significant risk factor for developing CAD (OR=3.33; 95%CI:1.95,5.68; p=0.0006). These findings were similar to study done by Vinay et al,[23] (2019) who also found that the risk of developing CAD is 3.3 times more among smokers compared to non-smokers. A study conducted by Rohit et al.[34] (2012) also found a significant association between tobacco smoking and CAD (OR =2.03 (95% CI:1.19-3.47) p<0.01).

In this study, it was found that smokeless tobacco use was present among 69 (53.08%) cases and 68 (52.31%) controls. We found no significant association between smokeless tobacco use and coronary artery disease. These findings were similar to the study conducted by Panwar et al.[35] (2011) who also found no significant association between smokeless tobacco use and CAD. On the contrary, study done Rohit et al.[34] (2012) found that there was a significant association between smokeless tobacco use and CAD (OR=2.06 (95%CI: 1.21-3.49) p= <0.01).

In this study, it was found that although alcohol consumption was more among cases compared to controls, there is no significant association between alcohol consumption and CAD (OR=1.08; 95%CI: 0.62,1.89; p=0.77). On the contrary, study conducted by Rohit et al.[34] (2012) found a significant association between alcohol consumption and CAD OR=2.31 (95% CI: 1.02-5.33) p<0.05. A study by Sharma et al.[36] (2017) found that alcohol intake was significantly associated with CAD [OR 3.5(95%CI:1.5-8.1) p<0.004].

In this study, it was found that there was no significant association between mixed diet intake and CAD (OR=1.13; 95%CI: 0.56,2.25; p=0.72). On the contrary, Tayyem et al.[37] (2017) found that there was a significant decrease in risk of developing CAD with a diet rich in fruits, vegetables and low meat intake [OR=0.53, (95%CI=0.28-0.98)]. In our study, it was found that physical activity <30min/d had a significant risk of developing CAD (OR=1.88; 95%CI:1.11,3.18; p=0.01). These findings were consistent with the study done by Mendagudli et al.[38] (2017) found that out of 93 CHD cases, 52 (55.91%) was sedentary and out of 1133 without CHD 499(44.04%) were sedentary and this difference was found to be significant. A study conducted by Rastogi et al.[39] (2003) found that people having leisure time exercise had a relative risk of 0.45(95%CI:0.31-0.66) for MI compared with non-exercisers.

In this study, screen time >2h/d was found to be a significant risk factor for developing CAD (OR=1.80; 95%CI:1.10,2.95; p=0.01). Kronenberg et al.[40] (2000) also observed that TV watching is significantly positively associated with triglycerides and cardiovascular disease (p=0.03). Grontved et al.[41] (2011) also observed that prolonged TV viewing >2h/d was significantly associated with type 2 diabetes and non-fatal cardiovascular disease.

Sleep duration ≤6h/d had no statistically significant association with CAD in our study (OR=1.32; 95%CI:0.81,2.16; p=0.26). These findings were similar to study done by Ayas et al.[42] (2003) who also found no significant association between sleep duration of 6h/d and CAD (OR:1.18;95%CI 0.98-1.42).

Mental stress (presence of >2 stressors during past 1year by PSLES) was not significantly associated with CAD in our study (OR=3.09; 95%CI:0.61,15.64; p=0.28). On the contrary, Gupta et al.[43] (2016) found that there is a significant difference in the mean number of stressful life events between Acute coronary syndrome (ACS) cases and controls.

In this study, it was found that there was no significant association between BMI ≥25kg/m^2 and CAD (OR=1.09; 95%CI:0.67,1.78; p=0.70). On the contrary, Ilic et al.[44] (2017) found that there was a significant association between BMI ≥25kg/m^2 and CAD (p=0.04).

In this study, it was found that among the metabolic risk factors, hypercholesterolemia (OR=3.53; 95%CI:1.36,9.17; p=0.006), hypertriglyceridemia (OR=2.84;95%CI:1.63,4.94; p=0.0001), high LDL cholesterol (OR=2.53; 95%CI: 1.52,4.19; p=0.0002) was found to be significantly associated with CAD. Similar findings were found in Hypertriglyceridemia was found to be significant risk factor for CAD [OR 2.58(95% CI: 1.43-4.66) p=0.002] in study done by Aggarwal et al.[45] (2012). A study conducted by Alsaqri et al.[46] (2020) also found a significant association between hypertriglyceridemia and CAD [OR 6.378 (95%CI 2.280-17.842) and p=0.000].

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Age (years)	**Cases**				**Controls**			
	Male		**Female**		**Male**		**Female**	
31-40	12	12.37	00	0.00	12	12.37	00	0.00
41-50	32	32.99	06	18.18	32	32.99	06	18.18
51-60	33	34.02	11	33.33	33	34.02	11	33.33
61-70	18	18.56	12	36.37	18	18.56	12	36.37
71-80	00	0.00	02	6.06	00	0.00	02	6.06
>80	02	2.06	02	6.06	02	2.06	02	6.06
Total	97	100.00	33	100.00	97	100.00	33	100.00

Table 1: Age and Gender-wise distribution of study subjects

Table 2: Association between risk factors and Coronary artery disease

Risk factors	**Cases No. (%)**	**Controls No. (%)**	**OR**	**95% CI**	**P value**
Diabetes mellitus					
Present	70 (53.8)	41 (31.5)	2.53	(1.52, 4.19)	0.0002*
Absent	60 (46.2)	89 (68.5)			
Hypertension					
Present	85 (65.4)	47 (36.2)	3.33	(2.00, 5.54)	0.0002*
Absent	45 (34.6)	83 (63.8)			
Tobacco smoking					
Yes	65 (50.0)	30 (23.08)	3.33	(1.95, 5.68)	0.006*
No	65 (50.0)	100 (76.92)			
Smokeless tobacco use					
Yes	69 (53.08)	68 (52.31)	1.03	(0.63, 1.67)	0.92
No	61 (46.92)	62 (47.69)			
Alcohol consumption					
Yes	34 (26.2)	32 (24.6)	1.08	(0.62, 1.89)	0.77
No	96 (73.8)	98 (75.4)			
Type of diet					
Mixed	112 (86.15)	110(84.62)	1.13	(0.56, 2.25)	0.72
Vegetarian	18 (13.85)	20(15.38)			
Physical activity					
<30min/d	52 (40.0)	34 (26.2)	1.88	(1.11, 3.18)	0.01*
≥30min/d	78 (60.0)	96 (73.8)			
Screen time					
>2h/d	70 (53.80)	51 (39.2)	1.80	(1.10, 2.95)	0.01*
≤2h/d	60 (46.20)	79 (60.8)			
Sleep duration					
≤6h/d	62 (47.7)	53 (40.8)	1.32	(0.81, 2.16)	0.26
>6h/d	68 (52.3)	77 (59.2)			
Mental stress					
>2 stressors	06 (4.61)	02 (1.54)	3.09	(0.61, 15.64)	0.28
≤2 stressors	124 (95.39)	128 (98.46)			
Obesity					
BMI ≥23	65 (50.0)	62 (47.69)	1.09	(0.67, 1.78)	0.70

BMI <23	65(50.0)	68 (52.31)			
Central obesity					
At risk	93 (71.54)	96 (73.85)	0.89	(0.51, 1.53)	0.67
No risk	37 (28.46)	34 (26.15)			

*P value <0.05 is significant

Table 3: Association between Lipid profile and coronary artery disease among study subjects

Lipid profile (mg/dl)	**Cases No. (%)**	**Controls No. (%)**	**OR**	**95% CI**	**P value**
Total cholesterol ≥200	19 (14.61)	06 (4.61)	3.53	(1.36, 9.17)	0.006*
Triglyceride ≥150	54(41.54)	26 (20.0)	2.84	(1.63, 4.94)	0.0001*
HDL ≤35	31(23.85)	30 (23.08)	1.04	(0.58, 1.85)	0.88
LDL ≥130	89(68.46)	60 (46.15)	2.53	(1.52, 4.19)	0.0002*

Table 4: Univariate analysis of risk factors associated with coronary artery disease

Risk factor	**Odds ratio**	**95% CI**	**P value**
Total cholesterol ≥200mg/dl	3.53	1.36, 9.17	0.006
Hypertension	3.33	2.00, 5.54	0.0002
Tobacco smoking	3.33	1.95, 5.68	0.0006
Family history of CAD	2.76	1.56, 4.86	0.0003
LDL cholesterol ≥130mg/dl	2.53	1.52, 4.19	0.0002
Diabetes mellitus	2.53	1.52, 4.19	0.0002
Physical activity <30min/d	1.88	1.11, 3.18	0.01
Screen time >2h/d	1.80	1.10, 2.95	0.01
Mental stress	3.09	0.61, 15.64	0.28
Sleep duration ≤6h/d	1.32	0.81, 2.16	0.26
Mixed diet	1.13	0.56, 2.25	0.72
Obesity: BMI≥23kg/m^2	1.09	0.67, 1.78	0.70
Alcohol consumption	1.08	0.62, 1.89	0.77
HDL cholesterol ≤35mg/dl	1.04	0.58,1.85	0.88
Smokeless tobacco use	1.03	0.63,1.67	0.90
Central obesity	1	0.47,2.09	0.99

WC (cm) ≥88(F)/≥102(M)			
Central obesity WHR ≥0.85(F)/≥0.95(M)	0.89	0.51, 1.53	0.67

Table 5: Multiple logistic regression analysis of risk factors for coronary artery disease

Risk factors	**AOR**	**95% CI**		**P value**
		Lower	**Upper**	
Tobacco smoking	3.23	1.81	5.76	0.000*
Hypertension	2.92	1.67	5.10	0.000*
Family history of CAD	2.83	1.49	5.38	0.001*
Diabetes mellitus	2.36	1.32	4.19	0.003*