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# Risk Factors of Coronary Artery Disease: A Hospital-Based Study

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## ABSTRACT

**Background:** Coronary artery disease is among the leading cause of morbidity and mortality worldwide. There are limited scientific evidence on the risk factors for coronary artery disease specific to the Nepalese context. This study aimed to determine the association of various modifiable cardiovascular risk factors with coronary artery disease in Nepal.

**Methods:** It is a hospital-based case-control study conducted among 300 participants. Case group comprised of 150 newly diagnosed coronary artery disease patients attending Manmohan Cardiothoracic Vascular and Transplant Centre while the Age and sex matched non-cardiac patients (n=150) from the outpatient department of the Department of General Practice and Emergency Medicine of Tribhuvan University Teaching Hospital were recruited as controls. Adjusted odds ratios (AOR) were calculated using multivariable logistic regression.

**Results:** Of the 300 participants, 208 (69.3%) were males and 92 (30.7%) were females. The mean age was 59.8 years ± 11 years (standard deviation). In multivariable analysis, current smoking (AOR=3.05, 95% CI: 1.61-5.78), hypertension (AOR=1.82, 95% CI: 1.08-3.09), diabetes (AOR=3.78, 95% CI: 1.91-7.47), family history of coronary artery disease (AOR=2.92, 95% CI: 1.27-6.71), and low high density lipoprotein (AOR= 2.0, 95% CI: 1.17-3.42) were significantly associated with coronary artery disease. Current alcohol use (AOR=0.51, 95% CI: 0.29-0.89) was identified as a protective factor for coronary artery disease.

**Conclusions:** Among the modifiable cardiovascular risk factors, smoking, hypertension, diabetes, and low level of high density lipoprotein were significantly associated with coronary artery disease, which should be considered while developing public health interventions for cardiovascular disease prevention in Nepal in future.

**Keywords:** Cardiovascular disease; coronary artery disease; Nepal

## INTRODUCTION

Coronary artery disease (CAD) is one of the leading causesof morbidity and mortality in both developing and developed countries.[1] Globally, smoking, dyslipidemia, hypertension, diabetes, central obesity and a positive family history have been identified as risk factors of CAD.[2-4]

Cardiovascular diseases have emerged as a major disease burden in developing countries.[5] Recently cardiovascular risk factors for ischemic heart disease and acute myocardial infarction are on the rise in Nepal.[6,7] However, well-defined studies analysing such an association in angiographically proven CAD patients in our country are lacking. This case-control study was conducted to determine an association of the above mentioned modifiable risk factors with CAD.

## METHODS

It was a hospital-based case-control study. Newly diagnosed CAD patients ≥18 years attending Manmohan Cardiothoracic Vascular and Transplant Centre (MCVTC) were consecutively selected as cases. After the performance of coronary angiography (emergency as well as elective) through the standard femoral or radial artery approach, angiograms were analyzed by two interventional cardiologists. CAD was defined as >1 epicardial coronary artery segment with stenosis >50% and was diagnosed visually. Controls were taken from every third non-cardiac patients attending outpatient department of the Department of General Practice and Emergency Medicine, Tribhuvan University Teaching

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Hospital (TUTH).

Frequencies of age and sex from cases were matched with control. Age matching was done with the liability of ± 2 years of age. Sample size was calculated using minimum odds to be detected as 2, percent of exposure among controls as 25.7%, power of test as 90%, level of significance (α) at 5% and case to control ratio as 1:1. The calculated sample size was 150 in each of the case and the control groups.

Data were collected by interviews, anthropometric measurements, clinical examinations, and biochemical measurements. The survey questionnaire covers the demographics and health behaviour of respondents. Demographic information includes the date of birth (age), sex, ethnicity, marital status, years at school and primary occupation. The health behaviour covered in the questionnaire includes tobacco use, alcohol consumption, and dietary salt consumption.

Tobacco use: Questions were asked to identify current users (those who were smoking tobacco in the past 30 days), daily users and past users.

Alcohol consumption: Questions were asked to determine the percentage of lifetime abstainers and current users of alcohol. Detailed information, such as the number of standard drinks consumed in the last 30 days, was obtained from current users. Pictorial cards showing different kinds of glasses and bowls most commonly used in Nepal were used to help the participants recall the amount of alcohol consumed. The amount reported was then used to calculate the number of standard drinks of alcohol consumed (one standard drink contains 10 grams of ethanol).

Diet: Data were collected from the participants on the frequency of fruit, vegetable and non-vegetarian diet consumption in the last six months duration. Dietary salt consumption was also assessed.

Physical activity: Physical activity related to work was categorised into vigorous, moderate and low levels of activity. Vigorous physical activity was defined as any activity that causes a significant rise in heart rate and breathing rate (for example digging or ploughing fields, lifting heavy weights, etc) continuously for at least 10 minutes. Moderate physical activity was defined as any activity that causes a moderate increment in heart rate and breathing rate (examples include domestic chores, gardening, lifting light weights, etc.) continuously for at least 30 minutes. Physical activity related to transport and recreation and time spent in sedentary behaviour was categorized as low level of activity.

Height and weight were measured, from which body mass index (BMI) was calculated. Height was measured with a portable standard stature scale after participants stood on a flat surface without footwear, with feet together and knees straight.

Blood pressure was measured with a Doctor's Aneroid Sphygmomanometer (BP Set) with a medium cuff size for all participants. Before taking the measurements, participants were asked to sit quietly and rest for 15 minutes with their legs uncrossed. Three readings of the systolic and diastolic blood pressure three minutes apart were taken. The mean of the second and third readings was calculated. Hypertension is defined as having systolic blood pressure ≥140 mm Hg and/or diastolic blood pressure ≥90 mm Hg during the study, or being previously diagnosed as having hypertension.

An already available hospital laboratory setting was used for biochemical analysis. First, the sample was collected, kept in an ice pack carrier and brought to the hospital laboratory within one hour. Participants were instructed to fast overnight for 12 hours and diabetic patients on medication were reminded to bring their medicine/insulin with them and take their medicine after providing the blood sample. A venous blood sample (4 ml of blood) was taken using a flashback needle with an aseptic technique and kept in plain and fluoride-treated tubes. Biochemical measurements of blood glucose and lipids were done using semi-automated procedures and commercially available kits. Plasma glucose was estimated using the GOD-PAP (glucose oxidase/peroxidase – phenol-4-amenophenazone) method. Serum total cholesterol was determined by an enzymatic endpoint method using the CHOD-PAP (cholesteroloxidase/peroxidase – 4-phenol-aminoantipyrine) method. Serum triglycerides were estimated using the GPO-PAP (glycerol-3-phosphate oxidase/peroxidase-4-chlorophenol and 4-aminophenazone) method. The determination of HDL cholesterol and low-density lipoproteins from the serum samples was first precipitated out. The clear supernatant was then analysed using the method described above for cholesterol.

Pretesting of the tool was done among 20 respondents. Amendment in questionnaires was applied as needed.

Data were entered in Epidata V.2.1 and analyzed in Stata V.16.0. Chi-square tests were conducted for comparing proportions of categorical variables. Odds ratios were calculated using binary logistic regression analysis.

Variables in multivariable analysis were selected based on the lowest possible values of Akaike's Information Criteria and Bayesian Information Criteria. All tests were two-tailed and *p*-value<0.05 was considered statistically significant.

Ethical approval was taken from Institutional Review Board, TUTH. Informed written consent was obtained from all the participants after explaining about research objectives, participants' role, autonomy, right to withdraw at any stage of the study, and privacy and confidentiality of information provided.

## RESULTS

Of the 300 participants, there were 208 (69.3%) were males and 92 (30.7%) were females. The mean age was 59.8 years ±11 years with a median of 60 years. Majority of them were from age groups of 50 to 60 years and 60-70 years with each group contributing one third of total participants. The majority of them belonged to Brahmin caste (39.9%). Approximately a hundred of them (29.4 %) had no formal education and 31.4% were homemakers. Nearly one-third of participants (29.7%) had 60 thousand and more household income per month (Table 1).

Table 1. Characteristics of research participants.

| Variables | Category | Case n (%) | Control n (%) | Total | p- value |
|---|---|---|---|---|---|
| Gender | Male | 104 (69.3) | 104 (69.3) | 208 (69.3) | 1.0 |
| | Female | 46 (30.7) | 46 (30.7) | 92 (30.7) | |
| Age Groups | <50 years | 21 (14) | 22 (14.7) | 43 (14.3) | 0.86 |
| | 50-60 years | 47 (31.3) | 50 (33.3) | 97 (32.3) | |
| | 60-70 years | 54 (36) | 47 (31.3) | 101 (33.7) | |
| | 70 years and above | 28 (18.7) | 31 (20.7) | 59 (19.7) | |
| Ethnicity | Brahman | 60 (40) | 62 (41.3) | 122 (40.7) | 0.33 |
| | Chhetri | 21 (14) | 26 (17.3) | 47 (15.7) | |
| | Newar | 30 (20) | 21 (14) | 51 (17) | |
| | Janajati other than Newar | 20 (13.3) | 28 (18.7) | 48 (16) | |
| | Others | 19 (12.7) | 13 (8.7) | 32 (10.7) | |
| Marital status | Married | 145 (96.7) | 132 (88) | 277 (92.3) | 0.09 |
| | Others (unmarired, widow) | 5 (3.3) | 18 (12) | 23 (7.7) | |
| Education | No formal education | 55 (36.9) | 33 (22) | 88 (29.4) | 0.01 |
| | Primary and lower | 25 (16.8) | 44 (29.3) | 69 (23.1) | |
| | Secondary | 41 (27.5) | 42 (28) | 83 (27.8) | |
| | Bachelor and higher | 28 (18.8) | 31 (20.7) | 59 (19.79) | |
| Occupation | Job | 29 (19.3) | 30 (20) | 59 (19.7) | 0.05 |
| | Self employed | 34 (22.7) | 27 (18) | 61 (20.3) | |
| | Homemaker | 46 (30.7) | 46 (30.7) | 92 (30.7) | |
| | Retired | 33 (22) | 24 (16) | 57 (19) | |
| | Others | 8 (5.3) | 23 (15.3) | 31 (10.3) | |
| Household income in NRs | <20000 | 35 (23.3) | 46 (30.7) | 81 (27) | 0.47 |
| | 20000-40000 | 39 (26) | 40 (26.7) | 79 (26.3) | |
| | 40000-60000 | 29 (19.3) | 24 (16) | 53 (17.7) | |
| | 60000 and above | 47 (31.3) | 40 (26.7) | 87 (29) | |

Among 150 cases, 67% had acute coronary syndrome (ACS) and the remaining 33% had chronic stable angina. Among the cases with ACS, 56% were presented with ST elevation MI and 23% had unstable angina. Most of the cases with chronic stable angina (85.7%) had TMT positive.

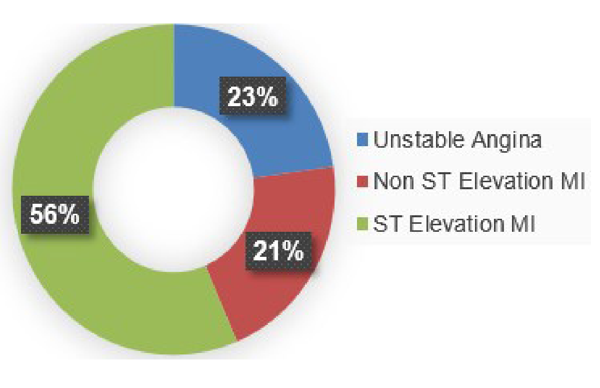


Figure 1. Types of coronary syndromes.

Similarly, nearly half of the cases (48%) were presented with single-vessel disease (SVD). The second-highest number (29%) belonged to double vessel disease (DVD), followed by triple vessel disease (TVD) with 21% and left main disease with 2%.

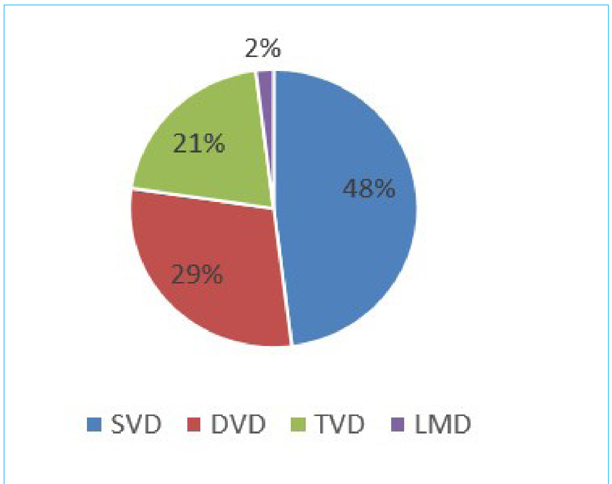


Figure 2. Types of CAD.

In coronary angiography, LAD (30.0%), RCA (10.0%), and LCX (4.7%) were the most common.

Among total participants, 76 (25.3%) were smoker until the last 30 days of the interview and 65 (21.7 %) reported they had quit smoking at the time of interview (past smoker) (Table 2).

Table 2. Distribution of the behavioural, metabolic and other factors.

| Variables | Category | Case n(%) | Control n (%) | Total N | p-value |
|---|---|---|---|---|---|
| Smoking | Non-smoker | 70 (46.7) | 89 (59.3) | 159 (53) | 0.03 |
| | Current smoker | 51 (34) | 25 (16.7) | 76 (25.3) | |
| | Past smokers | 29 (19.3) | 36 (24) | 65 (21.7) | |
| Alcohol | Non-alcoholic | 93 (62) | 68 (45.3) | 161 (53.7) | 0.01 |
| | Current user | 47 (31.3) | 64 (42.7) | 111 (37) | |
| | past user | 10 (6.7) | 18 (12) | 28 (9.3) | |
| Physical activity | Sufficient (≥600 METs/ week) | 72 (48) | 98 (65.3) | 170 (56.7) | 0.02 |
| | Not sufficient (<600 METs/ week) | 78 (52) | 52 (34.7) | 130 (43.3) | |
| Body mass index | <25 kg/ m2 | 77 (51.3) | 70 (46.7) | 147 (49) | 0.18 |
| | 25-29 kg/ m2 | 52 (34.7) | 66 (44) | 118 (39.3) | |
| | ≥30 kg/ m2 | 21 (14) | 14 (9.3) | 35 (11.7) | |
| Hyper-tension | No | 71 (47.3) | 95 (63.3) | 166 (55.3) | <0.01 |
| | Yes | 79 (52.7) | 55 (36.7) | 134 (44.7) | |
| Diabetes | No | 98 (65.3) | 136 (90.7) | 234 (78) | <0.01 |
| | Yes | 52 (34.7) | 14 (9.3) | 66 (22) | |
| Family history of CAD | Absent | 120 (80) | 140 (93.3) | 260 (86.7) | <0.01 |
| | Present | 30 (20) | 10 (6.7) | 40 (13.3) | |
| Total cholesterol | Low | 29 (19.3) | 45 (30) | 74 (24.7) | 0.03 |
| | High | 121 (80.7) | 105 (70) | 226 (75.3) | |
| HDL | High | 42 (28) | 75 (50) | 117 (39) | <0.01 |
| | Low | 108 (72) | 75 (50) | 183 (61) | |

A total of 111 (37%) participants had a history of drinking alcohol at least once in the past 30 days of time of interview. The average number of standard drinking in 30 days was 8.94 (not shown in table). Slightly less than half of participants (43.3%) were insufficiently (<600 METs) involved in moderate and vigorous physical activity. Higher proportion of cases than controls were involved in less physical activity. Obesity was relatively high in cases but was not statistically significant. Hypertension was present in 134 (44.7%) participants and diabetes was present in 22% of participants (Table 2).

Table 3. Obesity, blood pressure, lipid levels and blood sugar among cases and controls.

| Variables | Case | Control | P |
|---|---|---|---|
| | Mean ±SD | Mean ±SD | Value |
| BMI (kg/m2) | 25.5 ± 4.2 | 25.3 ± 3.9 | 0.63 |
| Waist circumference (cm) | 87.7 ± 10.3 | 88.2 ± 11.5 | 0.68 |
| Hip circumference (cm) | 86.3 ± 9.3 | 92.9 ± 14.3 | <0.01 |
| Waist Hip Ratio | 1.0 ± 0.1 | 0.95 ± 0.1 | <0.01 |
| Systolic BP | 125.1 ± 18 | 134.6 ± 20.2 | <0.01 |
| Diastolic BP | 79 ± 12 | 90.5 ± 16 | <0.01 |
| Fasting blood glucose | 116 ± 40 | 99.3 ± 29.3 | <0.01 |
| Total cholesterol | 166.59 ± 45.19 | 177.40 ± 43.24 | 0.04 |
| Triglycerides | 149.2 ± 87.7 | 149.6 ±70. | 0.96 |
| HDL | 44 ± 23.8 | 45.7 ± 25.1 | 0.54 |
| LDL | 99.5 ± 40.4 | 106.8 ± 32.3 | 0.08 |

The mean of hip circumference, waist hip ratio, systolic and diastolic BP, fasting blood glucose and total cholesterol varied significantly in case and control group (Table 3).

Multivariable analysis underscored smoking as a strong predictor of hypertension. Smokers had more than three times higher odds of having CAD than non-smokers. Similarly, the presence of a family history of CAD in first-degree relatives increased the odds of having CAD by almost three times. The odds of CAD was almost four times higher in participants with diabetes. In the case of low HDL, the odds of CAD was two times higher among those who had lower HDL level. Alcohol was identified as a protective factor for CAD (Table 4).

Table 4. Risk factors for CAD based on multivariable analysis.

| Variables | Category | Crude odds (95% CI) | Adjusted odds (95% CI) |
|---|---|---|---|
| Smoking | Non-smoker | Reference | Reference |
| | Current smoker | 2.59* (1.46-4.59) | 3.05* (1.61-5.78) |
| | Past smokers | 1.02 (0.57-1.83) | 1.16 (0.61-2.23) |
| Alcohol | Non-alcoholic | | |
| | Current user | 0.54* (0.33-0.88) | 0.51* (0.29-0.89) |
| | past user | 0.41* (0.18-0.94) | 0.47 (0.18-1.19) |
| Physical activity | Sufficient (≥600 METs/week) | Reference | |
| | Not sufficient (<600 METs/week) | 2.04* (1.28-3.25) | |
| Body mass index | <25 kg/m2 | Reference | |
| | 25-29 kg/m2 | 0.72 (0.44-1.17) | |
| | ≥30 kg/m2 | 1.36 (0.64-2.89) | |
| Hypertension | No | Reference | Reference |
| | Yes | 1.92* (1.21-3.05) | 1.82 (1.08-3.09) |
| Diabetes | No | Reference | Reference |
| | Yes | 5.15* (2.71-9.82) | 3.78* (1.91-7.47) |
| Family history of CHD | Absent | Reference | Reference |
| | Present | 3.5* (1.64-7.46) | 2.92* (1.27-6.71) |
| Cholesterol | Low | Reference | Reference |
| | High | 1.79* (1.05-3.05) | |
| HDL | High | Reference | Reference |
| | Low | 2.57* (1.59-4.15) | 2.0* (1.17-3.42) |

Note: * means significant at p<0.05; Final models included smoking, alcohol consumption, hypertension, diabetes, family history of CHD, and HDL cholestorol. Physical activity was removed from the model as it was strongly associated with hypertension as well as it did not have a significant association with CAD after adjusting its interaction with hypertension. Cholesterol was removed from the model as HDL was in the model.

## DISCUSSION

Among different CVD risk factors, hypertension was present in 44.7%, diabetes in 22%, high total cholesterol in 75.3% and low HDL cholesterol in 57.7%, smoking in 24.8% and low level of physical activity in 43%. Previous studies have also shown the high prevalence of these risk factors among adult Nepalese population.[8-10] Multivariable analysis showed the risk of CAD was higher among smokers, individuals with a family history of CAD, diabetic individuals and those having low HDL levels.

Our study revealed that the odds of CAD was almost 3 folds higher (OR=3.05, 95% CI 1.61 to 5.78) among participants with current smoking. Similar to the findings in our study, multiple previous studies have indicated the association with CAD.[11-14] Smoking is estimated to cause nearly 10% of all CVD.[12-15] Country should take initiative to reduce the burden of smoking, which could also reduce the burden of other CVDs and NCDs apart from CAD. One of the previous studies indicated that a restriction on the promotion of tobacco products, package labelling, implementation of smoke-free public places, media campaigns and increased taxation on tobacco products could reduce the prevalence of smoking and contribute to the prevention of different forms of CVDs. [16] One of the previous study also indicated that approximately 44.8% of current smokers had thought of quitting because of warning labels packages while 19.4% attempted to quit smoking. [17]

In our study, individuals with a family history of CAD were found to have almost 3 folds higher odds (OR: 2.92, 95% CI: 1.27 to 6.71) of CAD compared to those without any family history of CAD. Finding from our study aligns with that of a study by Jain et al.[18], which showed that a family history of premature CAD in first-degree relatives was associated with the development of CAD. Promoting regular health check-up and counselling individuals with a family history of CAD could be one option for the prevention and timely detection of CAD.

In bivariate analysis, low level of physical activity is associated with CAD (OR 2.04, 95% CI 1.28 to 3.25) which aligns with the finding reported by Thompson PD et al.[19]. The variable physical activity was not considered in multivariable analysis because of high collinearity with hypertension. Low level of physical may be acting through increased blood pressure in increasing the risk of CAD. Nepal should create a conducive environment that promotes physical activity among individuals. Setting up exercise rooms offices, encouraging cycling by setting up cycling lanes, setting up parks greeneries in different locations where individuals can do physical exercises like jogging, running, and playing can also be useful.

## CONCLUSIONS

Diabetes, hypertension, low physical activity level, low HDL and smoking were found as the factors significantly associated with CAD, which are also common risk factors for most other CVDs and NCDs. Reducing the burden of such risk factors could simultaneously reduce the risk of multiple types of CVDs.

## CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

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