

Prevalence and Risk Factors for Angina Pectoris and Coronary Heart Disease in the Dhulikhel  
Heart Study, Nepal

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A thesis submitted in partial fulfillment of requirements for the degree of

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Program Authorized to Offer Degree:

Global Health

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Abstract

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**Introduction:** Cardiovascular diseases (CVDs) account for approximately one-third of global mortality, with an estimated 20.5 million deaths in 2021. Coronary heart disease (CHD) onset was higher in South Asians. According to 2019 data, the leading cause of death in Nepal was cardiometabolic disease. Physiologically, atherosclerosis-related reduced oxygen-rich blood flow to the heart can result in angina and the age range in which angina is most likely to occur is between 45 and 65 years. Behavioral and lifestyle interventions, such as regular exercise, quitting smoking, and reducing alcohol consumption, can help prevent and manage patients with CHD and angina.

**Methods:** We conducted a cross-sectional study using secondary data from the Dhulikhel Heart Study (DHS) Wave 2, Nepal from June 2022 through July 2023. The total study sample size was 1608, in which adults (age 18 or older) residing in Dhulikhel Municipality, Kavre, Nepal, for more

than 6 months of settlement were enrolled. Data were collected in household interviews by trained research assistants including demographics, medical history, lifestyle behaviors, and selected health metrics (e.g. blood pressure, height, and weight, etc.). The primary outcomes of this study were angina pectoris and CHD, which were defined through self-reported variables using the Rose Angina Questionnaire. Angina was defined through a series of questions on chest pain occurrence and location of the pain. CHD was defined if either self-reported angina pectoris or myocardial infarction had been identified. Multivariable logistic regression was used to determine factors associated with angina and CHD in unadjusted and adjusted models which included age, gender (male/female), ethnicity (Brahmin, Chettri/ Newar/ others), religious status (non-Hindu/ Hindu), education (high school or more/ less than high school/no formal education), body mass index(normal/ underweight/overweight/obese), smoking behavior (never smoker/ former smoker/ current smoker). physical activity (low/moderate/ high), alcohol intake, (non-drinker/ current drinker), diet (healthy/ unhealthy), diabetes (yes/no), and hypertension (yes/no). We tested for effect modification of both outcomes using interactions of gender and ethnicity by the following covariates: age, education, BMI, smoking, and hypertension.

## **Results:**

***Angina Pectoris:*** In this sample, only 55 individuals, with a prevalence of 3.4%, were identified as having angina pectoris. In the full multivariable logistic regression model, angina was significantly associated with age, BMI, former smoking, alcohol intake, and hypertension. The odds of having angina were 1.05 times per year higher in participants with greater age (95% CI: 1.02–1.07,  $p < 0.001$ ). Individuals who were overweight were three times more likely to have angina (OR: 3.05, 95% CI: 1.48–6.29,  $p < 0.002$ ), and obese were almost five times more likely to have angina (OR: 4.92, 95% CI: 1.06–74.75,  $p < 0.04$ ) when compared to normal weight participants.

The odds of having angina were 4.17 times higher among former smokers (95% CI: 1.98–8.76,  $p < 0.001$ ) in comparison to those who never smoked. The association between hypertension and angina was impacted by the effect modification of gender.

**CHD:** CHD was self-reported in 123 individuals resulting in a prevalence of 7.6%. CHD was significantly associated with gender, education, BMI, smoking behavior, and dietary intake in fully adjusted multivariable logistic regression. In this sample, males had a lower risk of CHD than females, i.e. (males OR: 0.53, 95% CI: 0.32- 0.86,  $p < 0.01$ ), and those with education below high school level also had a reduced risk of CHD (OR: 0.39, 95% CI: 0.18- 0.81,  $p < 0.01$ ) than those who had more education. The odds of CHD were 1.69 times greater among overweight participants (95% CI: 1.07- 2.65,  $p$ -value 0.02), and 1.90 times higher among obese participants (95% CI: 1.09- 3.28,  $p < 0.02$ ) compared to normal weight participants. Former smokers were twice as likely to have reported CHD (OR: 2.35, 95% CI: 1.30–4.25,  $p < 0.004$ ) in comparison to those who never smoked. Those eating unhealthier diets had 1.90 times greater odds (95% CI: 1.20–3.00,  $p < 0.006$ ) of CHD compared with those who ate healthy diets.

**Effect Modification:** Only one significant interaction ( $p < 0.008$ ) was found in the tests conducted to identify effect modification between gender and hypertension in the angina model. Among males, the likelihood of reporting angina pectoris was higher if they had hypertension (OR: 4.66, 95% CI: 1.50-14.4,  $p < 0.008$ ) compared to those who did not have hypertension. In contrast, no such association was found among females. No, effect modification was observed in CHD models.

**Conclusion:** Our study found that angina pectoris was prevalent in 3.42% of our sample, and CHD had a prevalence of 7.65% generated from self-reported data in an urban population in Central Nepal. Angina was significantly associated with greater age, a higher BMI, former smoking, and drinking alcohol. Similarly, CHD was associated with age, male gender, unhealthy diet, being

obese and overweight, former smoking, and lower education. The prevalence of hypertension was found to increase the risk of angina only in male participants. These results document demographic and lifestyle factors related to these specific CVDs in the Nepalese population using household survey data. Interventions to address these cardiometabolic risk factors are needed to help reduce CVD and mortality due to heart disease in Nepal.

**Key Words:** *angina pectoris, coronary heart disease, Rose Angina Questionnaire, Dhulikhel Heart Study, cardiovascular disease*

## **Lists of Abbreviations**

**AP:** Angina Pectoris

**BMI:** Body Mass Index

**CHD:** Coronary Heart Disease

**CVD:** Cardiovascular Disease

**DBP:** Diastolic Blood Pressure

**DHS:** Dhulikhel Heart Study

**GBD:** Global Burden of Disease

**IHD:** Ischemic Heart Disease

**IHME:** Institute for Health Metrics and Evaluation

**KU:** Kathmandu University

**MET:** Metabolic Equivalent of Task

**MI:** Myocardial Infarction

**RAQ:** Rose Angina Questionnaire

**SBP:** Systolic Blood Pressure

**SCAPIS:** Swedish Cardiopulmonary Bioimage Study

**UW IRB:** University of Washington Institutional Review Board

**WHO:** World Health Organization

## Words of Acknowledgement

I would like to sincerely thank and appreciate a few people who have helped me along the way with this thesis, as their support and advice have been extremely helpful. First and foremost, I am deeply indebted to my thesis chair and advisor, Prof. Dr. Annette L. Fitzpatrick, and my committee members, Dr. Archana Shrestha (KU), and Dr. Sarah Masyuko (UW) from the Global Health Department, for all their advice, attention, and mentorship. This research has been shaped and I have been pushed toward excellence by their profound knowledge, insightful feedback, and meticulous attention to detail.

This journey hasn't been easy with the help of these personnel: Dr. Biraj Man Karmacharya and Dr. Archana Shrestha, who have been pillars in shaping me for this journey. My sincere gratitude goes to Mr. Dinesh Timalsena, Ms. Pramita Shrestha, and Ms. Bhawana Shrestha for their continuous guidance, encouragement, direction, assistance, and support in the entire field. I am grateful to the Cardiometabolic Research Training Program (CMRTP) and the IARTP Team for giving me this opportunity to pursue my academic journey. I am heartfully thankful to Prof. Dr. Carey Farquar, Ms. Adriane Bermann, Ms. Tesia Wood, Ms. Tanya Wunderlich, and Ms. Willa Goettling, who played a significant role in completing this thesis. In this period, I would also like to remember my guardian from Seattle, Mr. Kevin Fitzpatrick, and our lovely dog Greta.

I am immensely thankful to the Department of Global Health, the University of Washington, and my friends from Seattle. I'm obliged with gratitude to Dhulikhel Hospital-Kathmandu University Hospital for letting me enroll in the Dhulikhel Heart Study to complete this thesis requirement. I acknowledge all the participants in the Dhulikhel Heart Study (DHS) who were enrolled in wave 2. Your support has been indispensable, and I am forever thankful for your presence in my life.

I would like to dedicate this thesis to my parents, who nurtured me, supported me, contributed, and believed in my convictions for my academic and personal growth. I want to mention my mom and dad, my lovely wife Ms. Dipika Thapa, and my brother Mr. Prashant Khadka for their motivation to honor this degree.



Sincerely,  
Parashar Khadka

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## **Introduction**

Cardiovascular diseases (CVDs) are the world's leading cause of mortality, with an estimated 17.9 million deaths annually (1). Cardiovascular diseases (CVDs) are related to about one in three deaths globally. In 2021, there were an estimated 20.5 million deaths from CVDs, equating to 56,000 deaths per day, or approximately one death every 1.5 seconds (2). South Asians had a higher onset of coronary heart disease (CHD), and thus substantially higher increased risk of death in comparison to Whites (3). Data from the Institute of Health Metrics and Evaluation (IHME) 2019, showed that cardiometabolic disease was the primary cause of death in Nepal. Ischemic heart disease (IHD) was responsible for 12.27% of deaths, 7.8% of strokes, 1.8% of diabetes cases, 1.3% of hypertensive heart disease cases, and 2.6% of chronic kidney diseases (4). Ischemic heart disease is indicated by angina pectoris defined as a condition that makes heart muscles require more blood or oxygen resulting in chest pain (5). Risk factors associated with the onset of angina have been reported in the literature to include physical inactivity, psychological strain, intense temperatures, high-fat meals, binge alcohol consumption, and tobacco use (5). Physiologically, lack of oxygen-rich blood flow to the heart, a result of atherosclerosis, can cause angina (6). Angina is also known to be a precursor for other CVDs.

People between the ages of 45 and 65 are the most common age group to have angina onset. According to the Global Burden of Disease (GBD) 2015, 112 million people worldwide have angina, with nearly half going unrecognized by healthcare professionals (7). Twenty-six percent of cases were undiagnosed despite symptoms, carrying a three-fold higher risk of disability. In Western developed countries, males had a 1% annual incidence, slightly higher than females. The risk age group is 65 years for men and 70 years for women(8). Angina affects an estimated 54

million people worldwide, 16 million of whom reside in the WHO's Southeast Asia region, and its burden is rising (9). Treatment for angina pectoris involves changing one's lifestyle and managing risk factors, which includes eating a healthy diet, doing physical activity, and managing other medical conditions like diabetes, hypertension, obesity, and risk factors for cardiovascular disease (10). A prospective cohort study done in West UK between 1972 and 1976 with 20 years of follow-up reported that the risk of death, myocardial infarction, heart failure, and other cardiovascular events was significantly increased by angina during middle age (11).

Behavioral and lifestyle interventions, such as regular exercise, quitting smoking, and reducing alcohol consumption, can help prevent and manage patients with coronary heart disease (CHD) and angina (12). Similarly, nutritional interventions play a significant role in lowering the risk of CVD. Increased consumption of foods high in fiber, diets rich in fruits, vegetables, whole grains, nuts, and chicken, and increased consumption of plant proteins such as almonds, legumes, pumpkin seeds, and omega-3 fats can reduce the risk of heart disease. Other, lifestyle changes including regular exercise help control CVD, and reducing alcohol consumption helps lower blood pressure, diabetes, and triglycerides (13).

### **Definition**

Physiologically, lack of oxygen-rich blood flow to the heart, a result of atherosclerosis, can cause angina (14). Angina is defined as a type of chest pain that limits movement, is felt over the sternum or in the left arm and chest, and goes away in ten minutes or less with rest (15). CHD is defined as the accumulation of fat in the coronary arteries that causes blockage or interruption of the heart's blood supply (16). "The Rose Angina Questionnaire" (RAQ), a WHO-standardized screening tool, was created in 1962 to aid in the identification of ischemic heart pain (myocardial infarction,

coronary heart disease, and angina pectoris), particularly in epidemiological field surveys (17). The RAQ asks seven questions to determine whether a patient has angina and whether a myocardial infarction is possible in a single question (17). The questionnaire also helps to identify if a person is suffering from angina, MI as well as CHD. Cross-cultural adaptation of the RAQ within the South Asian context has been done with validation of the instrument in languages including Hindi, Urdu, Bengali, Punjabi(18), Arabic(19), Farsi(20), and Thai(21).

### **Specific Aims**

The specific aims of this study are:

- (1) To investigate the prevalence of angina pectoris (AP) and coronary heart disease (CHD) based on responses to the standardized Rose Angina Questionnaire (RAQ) in the suburban population of Dhulikhel Municipality, Nepal.
- (2) To assess the associated sociodemographic and behavioral risk factors for ischemic heart disease, indicated by angina and CHD.

## **Relevant Studies/ Literatures**

Angina pectoris as identified by the RAQ has been used in studies around the world to determine angina prevalence. Angina affects over 10% of Brazilians who are 18 years of age or older, according to a cross-sectional study done in 2019 by the National Survey of Health (22). The Northeast and North have a greater incidence of illness. Angina pectoris, which was more common in people with lower levels of education, was highly prevalent in the population (22). A study conducted in Sweden found that the prevalence of angina based on the RAQ questionnaire was 3.5%) among a cohort of 28,974 people (23). Similarly, the estimated national prevalence of chronic stable angina pectoris was 7.7% in Iran, according to data from the fourth round of the Surveillance of Risk Factors of Non-Communicable Diseases (SuRFNCD-2011) survey. They determined that the cause of this was underlying risk factors for CVD (24). In comparison to diagnoses made by cardiologists, a South Asian study discovered that the RAQ had a high specificity of 89% and a moderate sensitivity of 53% for identifying CHD in adult Bangladeshi patients (13). The prevalence of angina was 6.9% (95% CI: 5.4 – 8.4) in a cross-sectional study using the RAQ among adults aged 30-64 in Gampaha, Sri Lanka who had risk factors for CHD (25).

Studies on angina and CHD in Nepal are limited. A cross-sectional study in eastern Nepal in an urban population reported that tobacco use, age, and family history are key risk factors for CHD, with a prevalence of 3.6% angina among men aged 35 and older (26). The study, which included a sample size of 1,000, utilized the Rose Angina Questionnaire interpreted with Minnesota codes and employed a systematic random sampling technique. It was the first study in Nepal to measure angina pectoris in urban Nepal, although it was limited to male participants only. In this study, angina was found in 36 participants who reported a history of chest pain as well as having

previously been diagnosed with myocardial infarction (MI) or had undergone coronary-based interventions. Of these, 13 participants were found to have been diagnosed with MI. No other Nepalese studies to date have reported the prevalence of angina using epidemiologic research methods. However, a report by a team of cardiologists in Nepal indicated that CHD is significantly influenced by risk factors such as smoking, alcohol intake, physical inactivity, and poor diet. While the methodology was different from ours, it underscores the urgent need for preventive measures to reduce premature deaths and morbidity (27).

People in low- and middle-income nations are more likely to develop CVD at earlier ages. According to a study done in India between the 1960s and 2000, 3–4% of people in rural areas and 9–10% of people in urban areas had CHD (28). The risk of coronary artery disease is estimated to be 40% higher in South Asians than in other populations. (29) The prevalence of CVD has not been extensively studied in the existing literature.

### **Factors contributing to Angina Pectoris**

In a population-based in Sweden, the "Swedish Cardiopulmonary Bioimage Study (SCAPIS)," the prevalence of angina was found to be 3.5% based on the RAQ. Low educational attainment was identified as a significant risk factor for angina, with an odds ratio (OR) of 1.41 and a 95% confidence interval (CI) of 1.10 to 1.79. Additionally, other socio-demographic factors associated with angina included low income and unemployment (23).

Comparably, a population study carried out in Spain revealed that angina prevalence increased with CVD risk, with rates of 7.3% for men and 7.7% for women (30). Similarly, in a cross-sectional study using data from the Whitehall II study, women were more likely than men to have angina, with a prevalence of (4.4%) and (2.4%), respectively ( $p < 0.001$ ). The prevalence of

angina increased with age, specifically for males (1.8% for 35–39 years, 2.1% for 40–44 years, and 3.1% for 50–55 years) (p-value 0.004) (31).

According to a study done on 59,000 adults in India, (32) 4.69% of men and 7.02% of women had angina found from the RAQ questionnaire; the prevalence of hypertension was 28.71%, diabetes was 12.76%, smoking was 13.73%, 21.92% were overweight and 7.4% were obese based on BMI, and current alcohol users was 2.11%. Heart disease and angina were correlated with education level; angina was more common in the illiterate population 6.85%, whereas heart disease was more common in the highly educated (6.23%), and obesity (9.66%) was linked to heart disease. People over the age of 70 are twice as likely to develop heart disease (OR: 2.03, 95% CI: 1.79–2.29) as others. Angina was more common in women (OR: 2.03, 95% CI: 1.79–2.20), and compared to the illiterate population, the prevalence of angina was higher in those with diabetes (OR: 1.10, 95% CI: 0.99–1.23) and hypertension (OR: 1.67, 95% CI: 1.55–1.81) (32).

### **Factors Associated with CHD Prevalence**

According to a cross-sectional study of 45,000 US adults based on data from the National Health and Nutrition Examination Survey (NHANES), only 3.47% of participants had CHD, and the results indicated that there was a correlation between CHD and the risk of diabetes, angina, and hypertension. Males having lower educational status had a higher prevalence of CHD at 47.5% (33).

A cross-sectional study carried out in the Lebanese population over 40 years of age revealed that angina prevalence was 5.7% and that it was related to age, gender, hypertension, and diabetes. The study also revealed that males are more likely to have a high prevalence of CHD, with a prevalence

of (OR: 2.25, 95% CI 1.62-3.13), prevalent in participants with lower education (OR: 1.67, 95% CI: 1.21- 2.30). Multivariable analysis reveals that association with hypertension (OR: 2.64, 95% CI: 1.36- 5.11) (34).

A study conducted in Tabari, Iran, on a cohort population showed that the prevalence of CHD was found to be (9.2%). The study also suggested that the prevalence of CHD increased with age ( $p < 0.001$ ). Additionally, the prevalence of CHD was (11.2%) in the obese population, (8.8%) in the overweight population, and (7.5%) among cigarette smokers, Hypertension (20.9%) and diabetes (18.1%) (35).

A community-based study conducted in Delhi, India, found that the prevalence of CHD among the adult population (28.2%) in men and (22.4%) in women per 1,000 adults (25-64 years). CHD was diagnosed with the help of clinical history or treatment records in hospitals using the Minnesota code (36). Similarly, a study conducted on Turkish adults shows CHD prevalence was greater in men 5.8%, than in women, 5.0% (37).

Similarly, a study conducted in Sri Lanka showed a 7.3% reported prevalence of CHD among the age group 30-64 years, with associated risk factors such as obesity found at (44%), smoking behavior at (14.2%), and heavy alcohol intake at 11.4%. CVD diagnoses were made based on clinical history or treatment-confirmed hospital records using the Minnesota code for CHD (25). In another study done in Qazvin, Iran, the prevalence of CHD was linked to risk factors such as diabetes (12.8%), hypertension (9.6%), obesity (23.2%), and angina pectoris (2.2%) (38).

Pakistan conducted a cross-sectional study in the Karachi population, revealing the prevalence of risk factors for cardiovascular disease (CVD) to be (38.5%) for hypertension, (64.8%) in no

physical activity, (20.4%) current smokers, (18.5%) obesity, (9.1%) diabetes mellitus, and (33.7%) BMI overweight (39).

### **Need for Rose Angina and CHD Study in Nepal**

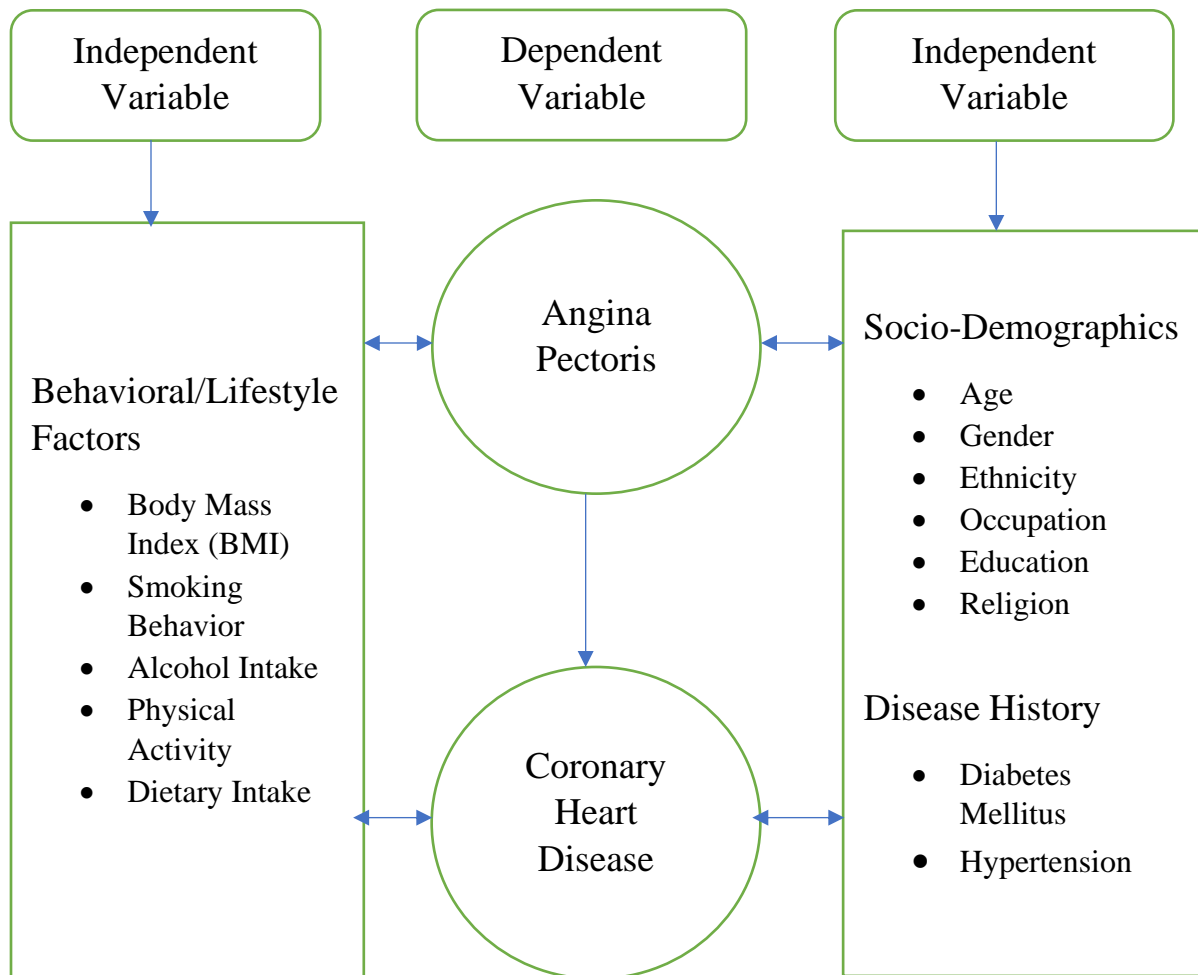
There is a great need to describe angina and CHD in Nepal. Due to large differences in prevalence reported in previous studies worldwide, using a standardized instrument like the RAQ can make prevalence rates more comparable. The RAQ helps to bridge the gaps by providing a consistent method for assessing angina across various populations.

The initial study in eastern Nepal investigated coronary heart disease (CHD) and angina for the first time using the Rose Angina Questionnaire (RAQ) and positive electrocardiographic changes based on Minnesota codes. However, this study only encompasses some genders and age groups, highlighting the need for a more comprehensive investigation that includes a broader demographic. Since this study, this research has yet to examine RAQ at the same level in detail.

We are using the RAQ questionnaire's information to assess the prevalence of angina and related risk - factors which help guide public health initiatives in Nepal that are aimed at preventing heart disease and promoting cardiovascular health. The results of this study have the potential to promote interventions for creating community-based screening programs, implementing lifestyle changes, and unveiling focused health education campaigns. This work will help address a larger gap in research on angina and CHD in community-based populations in low-resource settings. It also contributes to the early detection of people at risk of cardiovascular events by identifying people who have angina symptoms, a precursor to more serious outcomes including myocardial infarction. Increasing awareness of angina symptoms may help those at risk take prompt action and preventable steps to help lower Nepal's incidence of fatal CVD.

## Conceptual Framework

**Figure 1** defines the conceptual framework of our study variables. The primary outcomes, angina pectoris (AP) and coronary heart disease (CHD) are dependent variables. Risk factors influencing angina and CHD include age, gender, education status, body mass index, smoking habits, alcohol consumption, physical activity, and dietary patterns. Additionally, medical conditions such as diabetes and hypertension are represented in the diagram. Arrows indicate relationships between the variables.

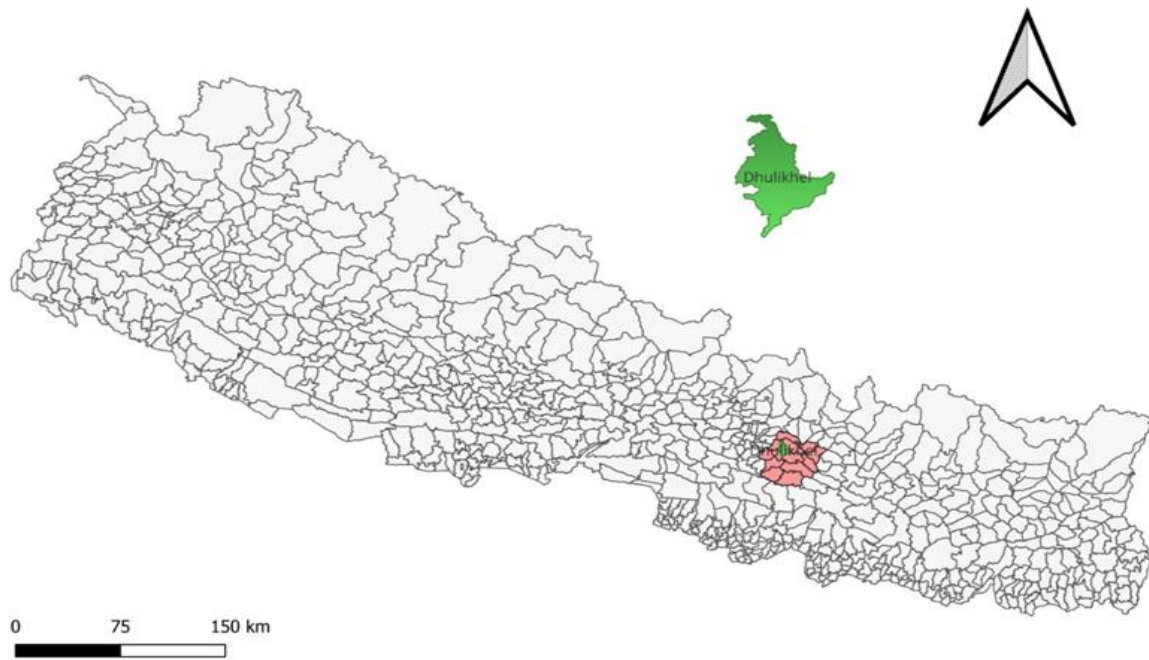


**Figure 1:** *Conceptual Framework of Study Variables*

## Research Methodology

**Study Design:** "This research describes a cross-sectional study using data collected by the Dhulikhel Heart Study (DHS) (40 – 43) Wave2. To investigate the trends of cardiovascular disease in Nepal, classified as a low-middle-income nation by the World Bank (44), the DHS was created as the first longitudinal study to evaluate and follow residents of Dhulikhel, Nepal. The first wave was carried out between 2013 and 2015. Wave 2 of DHS was conducted as the second phase of household data collection following the COVID-19 pandemic in 2022–23."

**Study Setting and Population:** The study population comprises of individuals residing in Dhulikhel Municipality, Kavre, Nepal (*Figure 2*), who were enrolled in the DHS in 2023. The DHS was an innovative research project of Dhulikhel Hospital of Kathmandu University Hospital. One-third of households were randomly selected for recruitment into the DHS. It was a complete sample, with all residents approached. Between June 2022 to July 2023: 1608, participants had been enrolled in Wave 2 of the DHS, which constituted the data for these analyses.



**Index: Wards of Dhulikhel Municipality (1- 12)**

**Figure 2:** Map of Dhulikhel Municipality, Nepal (45)

**Inclusion and Exclusion Criteria:** The inclusion criteria for DHS included all permanent household members aged > 18 years or older residing in Dhulikhel municipality for a minimum of 6 months who voluntarily signed informed consents and agreed to provide demographic and medical information to the research personnel. Temporary residents living in the Dhulikhel Municipality for less than six months and pregnant women were excluded from participation. The inclusion and exclusion criteria for these analyses were the same as those applied to the parent study. Only data from participants who completed the RAQ were extracted with missing observations removed for our study.

**Data Collection and Management:** The household field survey data were collected by trained and experienced research assistants who personally visited each household to recruit study participants. Convenience sampling was done to select household members above 18 years of age for providing household-level information. Each adult present was interviewed separately, and plans were made to return to the home to speak with any absent adult household members. The field activities were overseen by a program coordinator who reported directly to the principal investigator. Under the supervision of the principal investigator, their responsibilities encompassed training, setting up data instruments, evaluating data, and checking data completeness and quality. Data were synchronized with a computer-administered by the DHS research team and gathered via RED Cap 11.2 (46), on password-protected mobile devices (Android tablets). Project administrators checked the gathered data to ensure it was as complete as possible and corrected any errors or inconsistencies before sending it off for data cleaning and validation.

**Ethical Considerations:** This study received an IRB waiver from the University of Washington Division of Human Subjects as it used secondary data that had been de-identified (STUDY00020588). The DHS had previously received approval from the Nepal Health Research

Council and Kathmandu University School of Medical Sciences for study procedures under Protocol ID 63/13.

## Operational Definitions

*Table 1* lists the definitions for the terms used in this study. The wording of the RAQ questions and the use of responses to define angina, myocardial infarction, and CHD are also included.

**Table 1:** List of Operational Definitions

<b>Terminology</b>	<b>Definition</b>
<b>Angina Pectoris (AP)</b>	Chest pain or discomfort that recurs is known as angina pectoris or just angina. It occurs when there is insufficient blood flow and oxygen to a certain area of your heart (47).
<b>Myocardial Infraction (MI)</b>	When the heart muscle experiences a prolonged lack of oxygen supply, it can die irreversibly (necrosis), which is known as myocardial infarction (MI) or heart attack (48).
<b>Coronary Heart Disease (CHD)</b>	The accumulation of fat in the coronary arteries causes blockage or interruption of the heart's blood supply, which is known as coronary heart disease (16).
<b>Diabetes Mellitus (DM)</b>	The medical condition known as diabetes mellitus, or simply diabetes, is a long-term metabolic disease marked by elevated blood sugar levels, or hyperglycemia. It happens when the body is unable to use the insulin it does produce, or when it does not produce enough of it (49).
<b>Hypertension</b>	Hypertension also referred to as high blood pressure, is a medical condition in which there is a persistently high force of blood against the walls of arteries (50).

<b>Rose Angina Questionnaire (15)</b>	
Q.1. Within the last year, have you ever had a severe pain across the front of your chest lasting for half an hour or more?	Yes/ No
Q.2. Did the pain occur for the first time in the last year?	Yes/ No
Q.3. Within the last one year, have you ever had a pain or discomfort in your chest?	Yes/ No
Q.4. If no, on previous question, within the last one year, have you ever had any pressure or heaviness in your chest?	Yes/ No
Q.5. Did the pain/discomfort/pressure/heaviness in the chest occur for the first time in the last year?	Yes/ No
Q.6. Do you get it when you walk uphill or hurry?	Yes/ No
Q.7. Do you get it when you walk at an ordinary pace on the level?	Yes/ No
Q.8. What do you do if you get it while you are walking? (Probe)	Yes/ No
Q.9. If you stand still, what happens to it? (Probe)	Relieved/Not relieved
Q.10. Where do you get this pain or discomfort? (Write the code of the region)	(a) A (b) B (c) C (d) D (e) E (f) F <b>B &amp; E = Sternum</b> <b>C &amp; F = Left Anterior Chest &amp; Left Arm</b> <b>A &amp; D = Others</b>
<b>Angina Pectoris (AP)</b>	If (Q3 OR Q4=yes) AND (Q6 OR Q7=yes) AND (Q8=" stops or slows down" OR Q9=" relieved") AND (Q10= "sternum" or "left anterior chest and left arm") - check these locations. Then Rose Angina =1. Else Rose Angina=0.
<b>Myocardial Infraction (MI)</b>	If Q1=yes, MI=1. Else MI=0
<b>Coronary Heart disease (CHD)</b>	If MI=1 and Angina Pectoris=1, CHD=1. Else CHD=0.
<b>Hypertension</b>	Hypertension = (sbp>=140 or   dbp >=90   or medication = yes)

**Variables used in this study:** The outcomes in this study are angina pectoris (angina) and Coronary Heart Disease (CHD), which is based on the Rose Angina Questionnaire, (RAQ) (15), a standardized and validated tool to determine whether participants are having self-reported angina (15), myocardial infarction (MI) (15), or CHD (15). We will use potential confounders (socio-demographics (51), medical conditions (e.g. diabetes and hypertension) and behavioral and lifestyle factors (BMI , smoking behavior (52), alcohol intake, physical activity (53), and dietary intake (54) to determine associations with our outcomes angina and CHD.

*Table 2* provides details of variables used in our study.

**Table 2:** Socio- demographic, anthropometric, lifestyle, and medical history covariates used in this study.

Category	Variables	Descriptions
Socio- demographics	Age	Age (in completed years)
	Gender	Male/ Female
	Marital Status	Married/ Unmarried
	Occupational Status	Unemployed/Homemaker, retired/Student, Nonpaid, others/ Employed
	Religion	Hindu/ non-Hindu
	Ethnicity	Brahmin, Chettri/ Newar/ Others
	Education	High School or more/ Less than high school/ No formal education
	Income status	Sum Annual (in USD\$)
Anthropometric Measurement	Height	Kilogram (Kg)
	Weight	Centimeter (cm)
	Body Mass Index (BMI)	formula weight (in kg)/ (height in meters) <sup>2</sup> .
	Hypertension	Hypertension= if systolic bp is equal or greater than 140 mm/hg or diastolic bp is equal or greater than 90 or medication = yes)
CVD Risk Factors/ Behavioral Factors	Body Mass Index (BMI)	Underweight/Normal/ Overweight/ Obese

	Smoking behavior	Never Smoker/ Former Smoker/ Current Smoker
	Alcohol Intake	Standard drinks per week, Drinker: Non-drinker/ Current Drinker
	Physical Activity	GPAQ ( <i>Global Physical Activity Questionnaire</i> ) Low: (Less than 500 MET- minutes/ week)/ Moderate: (500- 2000 MET- minutes/ week) High: (> 2000 MET- minutes per week)
	Dietary Behavior	DQQ ( <i>Global Diet Quality Project</i> ) Unhealthy diet/ Healthy diet
Medical History	Diabetes Mellitus (DM)	No/ Yes (Self-reported).
	Hypertension	No/ Yes (as determined from anthropometrics described above).
Potential Confounders	<b><i>Sociodemographic</i></b> (age, gender, religion, occupational status, educational status) <b><i>Medical history</i></b> any co-morbidities (diabetes, hypertension, obesity) <b><i>Anthropometric measurement</i></b> of weight, height, BMI, blood pressure <b><i>CVD Risk factors</i></b> (smoking, alcohol intake, physical activity. Dietary pattern)	

**Data Analysis and Statistical Methods:** Statistical analysis was conducted using STATA 18.5 (55). For descriptive statistics, we calculated the means/standard deviations of continuous variables and frequencies (counts)/ percentages of categorical variables. The primary outcomes were angina pectoris and CHD, which were calculated using the validated Rose Angina Questionnaire (15). The predictors used in the study were socio-demographic variables (51) including age, gender (male or female), ethnicity (Brahmin, Chettri, Newar's, others), occupational status (unemployed, homemaker, retired, student, non-paid, or employed), religion (Hindu or non-Hindu), and educational status (more than high school, no education, or less than high school). Covariates considered as independent risk factors were diabetes (Yes/No) and hypertension

(Yes/No). Behavioral and lifestyle factors included BMI (obese/underweight/normal), smoking behavior (Former/current/never smoker) (52), alcohol intake (standard drinks per week, drinker type – Non- drinker/ current drinker) , physical activity (low: less than 500 MET per week, moderate: 500-2000 MET/week, high: greater than 2000 MET per week) (53), and diet (healthy/unhealthy diet) (54). Univariable and multivariable logistic regression models were used to assess whether there were associations between the outcome variables angina and CHD and the independent co-variates. Hierarchical adjustments were made using three models: unadjusted, adjusted for socio-demographics, and a full model with all other variables included. The results of the analysis were displayed as odds ratios (OR) with 95% confidence intervals (CI) and p-values.

To assess effect modification for both angina and CHD, we examined interactions between gender and ethnicity by the following variables: age, education status, body mass index (BMI), smoking characteristics, and hypertension. If the interactions were significant ( $p < 0.05$ ), stratified analyses by the relevant variables were conducted.

## Results

### 4. 1 Descriptive Characteristics of Study Population

#### Socio-Demographics

*Table 3* displays the socio-demographic characteristics of 653 males and 955 females in the study sample. The mean age was found to be similar for females and males, 46 years in both genders. There were more married participants 88.31% than unmarried. In terms of ethnicity, almost half were Brahmin 45.21%, followed by Newar 30.85%. Employee status differed by gender with 53.30% employed females compared to 71.36% employed males. Our participants were mostly Hindu, 91.29%, followed by other religions 8.71%. One-third, 33.1% of participants had no formal education, 43.1% did not complete high school, and only 23.13% had a high school degree or higher.

**Table 3:** Socio-demographic characteristics of the study participants (n = 1608)

<b>Variable</b>	<b>Female N= 955</b>	<b>Male N= 653</b>	<b>Total N= 1608</b>
<b>Age (in years), Mean±SD</b>	46.33 (16.70)	46.71 (17.13)	46.48 (16.80)
<b>Marital Status</b>			
Married	874 (91.52)	546 (16.39)	1420 (88.31)
Unmarried	81 (8.48)	107 (16.39)	188 (11.69)
<b>Ethnicity</b>			
Brahmin/ Chettri	436 (45.65)	291 (44.56)	727 (45.21)
Newar	291 (30.47)	205 (31.39)	496 (30.85)
Others	228 (23.87)	157 (24.04)	385 (23.94)
<b>Occupation Status</b>			
Unemployed	196 (20.52)	111 (17.00)	307 (19.09)
Homemaker/ retired	160 (16.75)	24 (3.68)	184 (11.44)
Student/ nonpaid/ others	90 (9.42)	52 (7.96)	142 (8.83)
Employed	509 (53.30)	466 (71.36)	975 (60.63)

<b>Religion</b>			
Hindu	871 (91.20)	597 (91.42)	1468 (91.29)
Non- Hindu	84 (8.80)	56 (8.58)	140 (8.71)
<b>Education</b>			
High school or more	173 (18.12)	199 (30.47)	372 (23.13)
Less than high school	342 (35.81)	351 (53.75)	693 (43.10)
No formal education	440 (46.07)	103 (15.77)	543 (33.77)
<b>Income (USD \$)</b>			
Income Annual, Mean±SD	485.77 (1759.53)	1717.76	10008.63
Ref: 1 USD \$ = 133 NRS		(5137.95)	(3593.71)

## 2. Behavioral/ Lifestyle Factors and Medical History of Participants in DHS

The distribution of cardiovascular risk factors among the study population by gender is shown in *Table 4*, providing information on the prevalence of these factors among the participants. In terms of BMI, it was found that 4.73% were underweight, 45.15% had a normal BMI, 34.51% were overweight, and 15.61% were classified as obese. While being overweight was equal between gender (34.46%), females had a higher prevalence of obesity (17.38%) than the males (13.02%).

Regarding smoking behavior, 13.78% of participants were former smokers, and 26.80% were current smokers. Males showed a higher prevalence of current smoking behavior (26.89%) compared to females (10.16%). Alcohol intake was calculated by measuring standard drinks per week and the majority were non- drinkers (85.57%). The prevalence of current drinking was higher among males (25.42%) compared to females (6.91%).

Physical activity levels were assessed based on a modification of the standardized WHO Global Physical Activity Questionnaire (GPAQ) criteria (53) based on Metabolic Equivalent of Time (METs) per week expended by participants. Overall, 28.61% of participants were categorized as having low physical activity, 13.87% as moderate, and 57.52% as high. Notably, both males and females showed similar rates of engaging in high physical activity (> 2000 METs per week).

Dietary habits indicated that 16.23% of participants had unhealthy diets, while 83.77% adhered to healthy diets. Regarding the history of health conditions, hypertension was prevalent in 36.07% of participants, whereas diabetes mellitus was less common, affecting 8.46% of the sample.

**Table 4:** Behavioral Factors and Medical History of Participants

<b>Variable</b>	<b>Female N= 955</b>	<b>Male N= 653</b>	<b>Total N= 1608</b>
<b>Body Mass Index (BMI)</b>			
Underweight	52 (5.45)	24 (3.68)	76 (4.73)
Normal	407 (42.62)	319 (48.85)	726 (45.15)
Overweight	330 (34.55)	225 (34.46)	555 (34.51)
Obese	166 (17.38)	85 (13.02)	251 (15.61)
<b>Smoking Behavior</b>			
Never Smoker	813 (85.13)	388 (59.42)	1201 (74.69)
Former Smoker	45 (4.71)	90 (13.78)	135 (8.40)
Current Smoker	97 (10.16)	175 (26.80)	272 (16.92)
<b>Type of drinker</b>			
Non- drinker	889 (93.09)	487 (74.58)	1376 (85.57)
Current drinker	66 (6.91)	166 (25.42)	232 (14.43)
<b>Alcohol Intake</b>			
Standard drinks per week, <b>Mean(±SD)</b>	0.041 (0.94)	0.287 (6.38)	0.141 (4.13)
<b>Physical Activity</b>			
Low (<500 MET mins/week)	275 (28.80)	185 (28.33)	460 (28.61)
Moderate (500- 2000 Met mins/week)	129 (13.51)	94 (14.40)	223 (13.87)
High (>=2000 MET mins/week)	551 (57.70)	374 (57.27)	925 (57.52)
<b>Dietary Intake</b>			
Healthy Diet ( <i>GDR score</i> ≥ 10)	800 (83.77)	547 (83.77)	1347 (83.77)
Unhealthy Diet ( <i>GDR score</i> < 10)	155 (16.23)	106 (16.23)	261 (16.23)
<b>Diabetes Mellitus (DM)</b>			
No	880 (92.71)	592 (90.66)	1472 (91.54)
Yes	75 (7.85)	61 (9.34)	136 (8.46)
<b>Hypertension</b>			
No	649 (67.96)	379 (58.04)	1028 (63.93)
Yes	306 (32.04)	274 (41.96)	580 (36.07)

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\*\*\*"The GPAQ guidelines given by WHO categorize physical activity levels as follows: Low: Less than 600 MET-minutes/week, Moderate: 600 to 1499 MET-minutes/week, and High: More than 1500 MET-minutes/week. We adjusted our physical activity categories slightly to reflect the distribution in our sample."

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### 3. Cardiovascular Disease Prevalence

**Table 5** provides an overview of the prevalence of angina pectoris, myocardial infarction (MI), and coronary heart disease (CHD) within our sample. This table details the presence and absence of these conditions, presented as both counts and percentages. In our sample of 1,608 participants, we observed the prevalence of angina to be 3.42%. The prevalence of CHD (which includes the RAQ prevalence of angina or MI) was 7.65%.

**Table 5:** CVD Prevalence

Characteristics*	n (%)
<b>Angina Pectoris (AP)</b>	
No Rose Angina	1553 (96.58)
Having Angina	<b>55 (3.42)</b>
<b>Myocardial Infraction (MI)</b>	
No MI	1503 (93.47)
Having MI	105 (6.53)
<b>Coronary Heart Disease (CHD)</b>	
No CHD	1485 (92.35)
Having CHD	<b>123 (7.65)</b>

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*\*\*Note: This is self reported data based on responses to the RAQ.*

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## 4.2 Regression Analysis

### Associations with Angina Pectoris

We conducted univariable and multivariable logistic regression analyses to determine the associations of socio-demographic characteristics, behavioral characteristics, and medical history with the presence of angina pectoris (*Table 6*). In the unadjusted models, we found that angina was significantly associated with age, education, body mass index, and smoking behavior. The odds of having angina were 1.04 times higher per year in participants (95% CI: 1.03 – 1.06,  $p < 0.001$ ). Education resulted in a J-shaped risk relative to those with a high school education or higher. The odds of having angina were reduced (OR: 0.86) in those who had attained education up to high school (95% CI: 0.11–0.64,  $p < 0.01$ ) and 2.07 times higher among those who had not attained any formal education (95% CI: 1.18–3.62,  $p < 0.01$ ). The odds of having angina pectoris were 2.29 times higher among overweight participants (95% CI: 1.17–4.48,  $p < 0.01$ ) and 3.46 times higher among participants with obesity (95% CI: 1.66– 7.20,  $p < 0.001$ ) as compared to those with normal weight. The odds of having angina were 5.24 times higher among former smokers (95% CI: 2.78, 9.90,  $p < 0.001$ ) compared to those who never smoked.

In model 2, adjusted for socio-demographic variables, we found that angina was significantly associated with age, education, BMI, smoking behavior, and alcohol intake. The odds of having angina were 1.03 times higher per year in participants with greater age (95% CI: 1.01–1.06,  $p < 0.001$ ). The odds of having angina were 2.71 times higher among overweight participants (95% CI: 1.36, 5.40,  $p < 0.004$ ) and 4.11 times higher among obese participants (95% CI: 1.91–8.86,  $p < 0.001$ ) when compared with normal weight participants. The odds of having angina were 4.20 times higher among former smokers (95% CI: 2.08, 8.50,  $p < 0.001$ ) compared to those who never smoked.

In model 3, the full model, we adjusted for socio-demographic, behavioral characteristics and medical history of the participants. We found that angina pectoris was significantly associated with age, smoking behavior, alcohol intake and hypertension. The odds of having angina pectoris were 1.05 times per year higher in participants with greater age (95% CI: 1.02–1.07,  $p < 0.001$ ). The odds of having angina were 3.05 times greater among participants with overweight (95% CI: 1.48–6.29,  $p < 0.002$ ) and 4.92 times higher among obese participants (95% CI: 2.18–11.09,  $p < 0.0001$ ) when compared to normal weight participants. The odds of having angina were 4.17 times higher among former smokers (95% CI: 1.98–8.76,  $p < 0.001$ ) in comparison to those who never smoked. Results of associations with hypertension were modified by gender and the OR less than 1.0 is not an accurate reflection of the associated risk. Effect modification is described later in Results.

**Table 6:** Factors associated with Angina Pectoris in unadjusted and adjusted models (n= 1608)

Characteristics	*Model 1*			*Model 2*			*Model 3*		
	Unadjusted			Adjusted for socio-demographic variables			Adjusted for socio- demographic, behavioral characteristics, and medical history		
Outcome: Angina Pectoris	(n= 1608)			(n= 1608)			(n= 1608)		
Variables	OR	95% CI	p value	OR	95% CI	p value	OR	95% CI	p value
<b>Age</b>	1.04	(1.03, 1.06)	<0.001	1.03	(1.01, 1.06)	<0.001	1.05	(1.02, 1.07)	<0.001
<b>Gender</b>									
Female	<b>Ref</b>			<b>Ref</b>			<b>Ref</b>		
Male	0.64	(0.36, 1.15)	0.13	0.73	(0.38, 1.40)	0.34	0.52	(0.25, 1.10)	0.09
<b>Ethnicity</b>									
Brahmin/Chettri	<b>Ref</b>			<b>Ref</b>			<b>Ref</b>		
Newar	1.34	(0.72, 2.49)	0.34	1.22	(0.64, 2.31)	0.53	0.90	(0.44, 1.84)	0.79
Others	1.11	(0.55, 2.24)	0.75	1.36	(0.65, 2.87)	0.41	0.97	(0.43, 2.19)	0.95
<b>Religion Status</b>									
Non-Hindu	<b>Ref</b>			<b>Ref</b>			<b>Ref</b>		
Hindu	1.67	(0.51, 5.44)	0.38	1.64	(0.47, 5.64)	0.43	1.58	(0.43, 5.74)	0.48
<b>Educational Status</b>									
High School or More	<b>Ref</b>			<b>Ref</b>			<b>Ref</b>		
Less than high school	0.08	(0.11, 0.64)	<b>0.01</b>	0.13	(0.01, 1.01)	<b>0.05</b>	0.15	(0.20, 1.20)	0.07
No formal education	2.07	(1.18, 3.62)	<b>0.01</b>	1.05	(0.51, 2.15)	0.89	0.96	(0.46, 2.03)	0.93

**Body Mass Index (BMI)**

Normal	<b>Ref</b>			<b>Ref</b>			<b>Ref</b>		
Underweight	0.67	(0.87, 5.22)	0.70	0.66	(0.08, 5.29)	0.70	0.55	(0.06, 4.51)	0.58
Overweight	2.29	(1.17, 4.48)	<b>0.01</b>	2.71	(1.36, 5.40)	<b>0.004</b>	3.05	(1.48, 6.29)	<b>0.002</b>
Obese	3.46	(1.66, 7.20)	<b>0.001</b>	4.11	(1.91, 8.86)	<b>&lt;0.001</b>	4.92	(2.18, 11.09)	<b>0.0001</b>

**Smoking Behavior**

Never Smoker	<b>Ref</b>			<b>Ref</b>			<b>Ref</b>		
Former Smoker	5.24	(2.78, 9.90)	<b>&lt;0.001</b>	4.20	(2.08, 8.50)	<b>&lt;0.001</b>	4.17	(1.98, 8.76)	<b>&lt;0.001</b>
Current Smoker	1.33	(0.62, 2.84)	0.45	1.19	(0.53, 2.64)	0.66	1.34	(0.56, 3.20)	0.50

**Physical Activity\*\***

Low (Less than 500 MET Per Week)	<b>Ref</b>			<b>Ref</b>			<b>Ref</b>		
Moderate (500-2000 MET)	0.47	(0.17, 1.28)	0.14	0.58	(0.21, 1.60)	0.29	0.55	(0.19, 1.56)	0.26
High (<2000 MET)	0.67	(0.38, 1.20)	0.18	0.92	(0.49, 1.71)	0.79	1.02	(0.53, 1.94)	0.95

**Alcohol Intake****Type of drinker**

Non- Drinker	<b>Ref</b>			<b>Ref</b>			<b>Ref</b>		
Current Drinker	1.69	(0.87, 3.25)	0.11	2.03	(0.97, 4.25)	<b>0.05</b>	2.16	(0.98, 4.80)	<b>0.05</b>

**Dietary Intake**

Healthy Diet	<b>Ref</b>			<b>Ref</b>			<b>Ref</b>		
Unhealthy Diet	1.62	(0.86, 3.07)	0.13	1.69	(0.87, 3.27)	0.11	1.61	(0.80, 3.22)	0.17

**Diabetes Mellitus (DM)**

No	<b>Ref</b>			<b>Ref</b>			<b>Ref</b>		
Yes	1.89	(0.87, 4.09)	1.62	1.08	(0.48, 2.40)	0.84	1.16	(0.50, 2.72)	0.72

**Hypertension**

No	<b>Ref</b>			<b>Ref</b>			<b>Ref</b>		
Yes	1.38*	(0.80, 2.38)	0.23	0.74***	(0.41, 1.35)	0.33	0.45***	(0.23, 0.87)	<b>0.01</b>

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Bold p values indicate significance at a 5% level of significance.

\*Model 1: Unadjusted associations of AP with independent variables; Model 2: AP Adjusted for sociodemographic variables (age, gender, ethnicity, religion, education); Model 3: Adjusted for sociodemographic (model 2) plus behavioral factors and medical history (BMI, smoking behavior, physical activity, alcohol intake, type of drinker, diabetes, hypertension).

\*\*PA: GPAQ guidelines Low: < 600 MET-minutes/week; moderate: 600–1500 MET-minutes/week; and high: > 1500 MET-minutes/week. physical activity adjusted in our study to make analytically suitable revisions of ranges."

\*\*\*Effect modification by gender influenced these results.

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## **Associations with Coronary Heart Disease (CHD)**

We conducted univariable and multivariable logistic regression analyses to determine the associations of socio-demographic characteristics, behavioral characteristics, and medical history with the presence of coronary heart disease (CHD) (*Table 7*). In the unadjusted models, we found that CHD was significantly associated with age, gender, education, body mass index, smoking behavior and diet. The odds of having CHD were 1.02 times higher in participants with greater age (95% CI: 1.01 – 1.03,  $p < 0.001$ ). The odds of having CHD were lower for males versus females (OR: 0.60, 95% CI: 0.40- 0.90,  $p 0.01$ ). Our data showed that those with education below high school had a reduced odds of having CHD (OR: 0.34, 95% CI: 0.17– 0.67,  $p 0.002$ ) and increased odds for those who had not attained any formal education (OR: 1.56, 95% CI: 1.05 – 2.30,  $p 0.02$ ) compared to those who had attained a high school or higher education. The odds of having CHD were 1.75 times higher among obese participants (95% CI: 1.04 – 2.94,  $p 0.03$ ) and 2.50 times higher among former smokers (95% CI: 1.47, 4.24,  $p < 0.001$ ) compared to those who never smoked. The odds of having CHD were 1.75 times higher among healthy diet participants (95% CI: 1.13 – 2.70,  $p 0.01$ ) compared with those who ate healthy diets.

In model 2, we adjusted for socio-demographic variables and found, similar to model 1, that CHD was significantly associated with age, education, BMI, smoking behavior, and diet. The odds of having CHD were 1.01 times higher per year in participants with greater age (95% CI: 1.00–1.03,  $p 0.03$ ). For education, odds of having CHD were 0.40 times lower among those who had attained education below high school (95% CI: 0.19– 0.82,  $p 0.01$ ) as compared to those with high school or higher although associations with no formal education were no longer present. The odds of having CHD were 1.64 times higher among overweight participants (95% CI: 1.06, 2.55,  $p 0.02$ ) and 1.77 times higher among obese participants (95% CI: 1.04 – 3.01,  $p 0.03$ ) when compared

with normal weight participants. The odds of having CHD were 2.50 times higher among former smokers (95% CI: 1.40- 4.45, p 0.002) compared to those who never smoked. Persons eating an unhealthy diet were 1.92 times more likely to have CHD. (OR: 1.92, 95% CI: 1.23 – 3.01, p 0.004).

In model 3, adjusted for all variables, age was no longer associated with CHD due to the adjustment of one or more of the other included variables. We found that CHD remained significantly associated with gender, education, BMI, smoking behavior and dietary intake. In our data, males had a lower risk of CHD than females. The odds of having CHD were 0.53 times lower among males (95% CI: 0.32- 0.86, p 0.01) as compared to female participants. Other associations were similar to the previous models. Those with education below high school level had odds of CHD 0.39 times lower (95% CI: 0.18– 0.81, p 0.01) than those who had more education. The odds of having CHD were 1.69 times greater among overweight participants (95% CI: 1.07– 2.65, p 0.02) and 1.90 times higher among obese participants (95% CI: 1.09–3.28, p 0.02) when compared to normal weight participants. The odds of having CHD were 2.35 times higher for former smokers (95% CI: 1.30– 4.25, p-value 0.004) in comparison to those who never smoked. Those eating unhealthier diets had 1.90 times greater odds (95% CI: 1.20 – 3.00, p 0.006) of CHD compared with those who ate healthy diets.

**Table 7:** Factors associated with coronary heart disease in unadjusted and adjusted models (n= 1608)

Characteristics	*Model 1*			*Model 2*			*Model 3*		
	Unadjusted			Adjusted for socio- demographic variables			Adjusted for socio- demographic, behavioral characteristics, and medical history		
	(n= 1608)			(n= 1608)			(n= 1608)		
Variables	OR	95% CI	p-value	OR	95% CI	p value	OR	95% CI	p value
<b>Age</b>	1.02	(1.01, 1.03)	<b>&lt;0.001</b>	1.01	(1.00, 1.03)	<b>0.03</b>	1.01	(0.99, 1.03)	0.06
<b>Gender</b>									
Female	<b>Ref</b>			<b>Ref</b>			<b>Ref</b>		
Male	0.60	(0.40, 0.90)	<b>0.01</b>	0.66	(0.42, 1.03)	0.07	0.53	(0.32, 0.86)	<b>0.01</b>
<b>Ethnicity</b>									
Brahmin/Chettri	<b>Ref</b>			<b>Ref</b>			<b>Ref</b>		
Newar	0.96	(0.62, 1.48)	0.87	0.91	(0.58, 1.42)	0.69	0.73	(0.45, 1.18)	0.20
Others	1.01	(0.63, 1.60)	0.95	1.16	(0.71, 1.91)	0.53	0.95	(0.56, 1.61)	0.87
<b>Religion Status</b>									
Non-Hindu	<b>Ref</b>			<b>Ref</b>			<b>Ref</b>		
Hindu	1.93	(0.83, 4.47)	0.12	2.09	(0.87, 5.04)	0.09	2.13	(0.86, 5.24)	0.10
<b>Educational Status</b>									
High School or More	<b>Ref</b>			<b>Ref</b>			<b>Ref</b>		
Less than high school	0.34	(0.17, 0.67)	<b>0.002</b>	0.40	(0.19, 0.82)	<b>0.01</b>	0.39	(0.18, 0.81)	<b>0.01</b>
No formal education	1.56	(1.05, 2.30)	<b>0.02</b>	1.05	(0.64, 1.72)	0.83	0.95	(0.57, 1.59)	0.85

**Body Mass Index (BMI)**

Normal	<b>Ref</b>			<b>Ref</b>			<b>Ref</b>		
Underweight	1.61	(0.69, 3.71)	0.26	1.69	(0.72, 3.98)	0.22	1.56	(0.65, 3.74)	0.31
Overweight	1.50	(0.98, 2.30)	0.06	1.64	(1.06, 2.55)	<b>0.02</b>	1.69	(1.07, 2.65)	<b>0.02</b>
Obese	1.75	(1.04, 2.94)	<b>0.03</b>	1.77	(1.04, 3.01)	<b>0.03</b>	1.90	(1.09, 3.28)	<b>0.02</b>

**Smoking Behavior**

Never Smoker	<b>Ref</b>			<b>Ref</b>			<b>Ref</b>		
Former Smoker	2.50	(1.47, 4.24)	<b>&lt;0.001</b>	2.50	(1.40, 4.45)	<b>0.002</b>	2.35	(1.30, 4.25)	<b>0.004</b>
Current Smoker	1.45	(0.90, 2.33)	0.11	1.44	(0.86, 2.40)	0.16	1.46	(0.84, 2.52)	0.17

**Physical Activity**

Low (Less than 500 MET Per Week)	<b>Ref</b>			<b>Ref</b>			<b>Ref</b>		
Moderate (500-2000 MET)	0.74	(0.41, 1.36)	0.34	0.78	(0.42, 1.44)	0.44	0.79	(0.42, 1.47)	0.47
High (<2000 MET)	0.72	(0.48, 1.07)	0.11	0.76	(0.49, 1.16)	0.20	0.77	(0.50, 1.20)	0.25

**Alcohol Intake****Type of drinker**

Non- Drinker	<b>Ref</b>			<b>Ref</b>			<b>Ref</b>		
Current Drinker	1.24	(0.76, 2.03)	0.38	1.51	(0.88, 2.61)	0.13	1.51	(0.85, 2.69)	0.15

**Dietary Intake**

Healthy Diet	<b>Ref</b>			<b>Ref</b>			<b>Ref</b>		
Unhealthy Diet	1.75	(1.13, 2.70)	<b>0.01</b>	1.92	(1.23, 3.01)	<b>0.004</b>	1.90	(1.20, 3.00)	<b>0.006</b>

<b>Diabetes Mellitus (DM)</b>									
No	<b>Ref</b>			<b>Ref</b>			<b>Ref</b>		
Yes	1.70	(0.97, 2.97)	0.06	1.30	(0.73, 2.33)	0.36	1.36	(0.74, 2.48)	0.31
<b>Hypertension</b>									
No	<b>Ref</b>			<b>Ref</b>			<b>Ref</b>		
Yes	1.18	(0.81, 1.73)	0.36	0.91	(0.60, 1.38)	0.66	0.73	(0.47, 1.14)	0.17

Bold p values indicate significance at a 5% level of significance.

\*Model 1: Unadjusted associations of AP with independent variables; Model 2: AP Adjusted for sociodemographic variables (age, gender, ethnicity, religion, education); Model 3: Adjusted for sociodemographic (model 2) plus behavioral factors and medical history (BMI, smoking behavior, physical activity, alcohol intake, type of drinker, diabetes, hypertension).

\*\*PA: GPAQ guidelines Low: < 600 MET-minutes/week; moderate: 600–1500 MET-minutes/week; and high: > 1500 MET-minutes/week. physical activity adjusted in our study to make analytically suitable revisions of ranges."

\*\*\*Effect modification by gender influenced these results.

## Effect Modification in Angina Pectoris and Coronary Heart Disease (CHD)

We tested for effect modification for our outcomes, angina and CHD, for interactions between gender and ethnicity with the following variables: age, education status, body mass index BMI, smoking characteristics, diet and hypertension.

We found a significant interaction for angina pectoris between hypertension and gender ( $p=0.008$ ). Specifically, males showed a significantly higher likelihood of having angina in those who had hypertension (OR: 4.66, 95% CI: 1.50-14.4,  $p=0.008$ ), whereas no such association was found among females. Conversely, no effect modification was observed for any other variables in association with angina nor interactions with CHD.

**Table 8:** shows results of the stratified analysis. Unfortunately, our study faced limitations due to a small sample size and only unadjusted models are shown.

Table 8: Angina Pectoris Effect Modification of Hypertension by Gender				
	Category	O. R	95% CI	P value
<b>Males, n = 653</b>				
	No Hypertension	<b>Ref.</b>		
	Hypertension	4.66	(1.50, 14.40)	<b>0.008</b>
<b>Females, n = 955</b>				
	No Hypertension	<b>Ref.</b>		
	Hypertension	0.85	(0.42, 1.75)	0.67

*Bold p values indicate significance at a 5% level of significance.*

## **Discussion**

In this study, we analyzed the data collected from the Dhulikhel Heart Study (DHS), a population-based study conducted among sub-urban Nepalese adults residing in Dhulikhel municipality, Nepal. This study determined the prevalence of angina and CHD and associated risk factors. Overall, the prevalence of angina was found to be 3.42% and the prevalence of CHD, which includes both angina and MI, was 7.65%. Our study found that angina was associated with age, education status, BMI (overweight or obese), smoking behavior, alcohol intake, and hypertension (modified by gender). Similarly, CHD was found to be associated with age, gender, education, BMI (overweight), BMI (obesity), smoking behavior, and dietary intake. Effect modification was found for angina in that hypertension increased the risk of angina in males but not in females.

Very few studies have explored the prevalence of angina and CHD in Nepal. Despite the lack of national data, there is a high burden of CHD and angina in Nepal. The first study in Nepal to assess the prevalence of angina and CHD was conducted by Vaidya et al. in 2009 (26). This study found that 36 out of 1,000 male participants (3.6%) were diagnosed with angina using the RAQ, prevalence much similar to our study. Our study, which included 1,608 participants, identified 55 cases of angina, or 3.42%. For CHD, the Dharan study reported a prevalence of 5.7%, while our study found a prevalence of 7.65%. The Dharan study was the first study in Nepal focused on males over 35 with angina risk; our study included both males and females over 18 years of age. No other Nepalese studies have provided data on the prevalence of angina in a large population that included both genders. Thus, the DHS study plays a significant role in filling this gap. There is a lack of national data on this topic, and our study will significantly contribute to the field by providing valuable information for future research on the prevalence of angina and CHD categorized by RAQ tool.

A study in Nepal shows that the population-based prevalence of coronary artery disease in the age group of 20 years and older was found to be 2.90% (56). CHD is always a prime contributor to mortality and the risk factors are associated with it, including smoking intake, alcohol consumption, physical inactivity as well as poor diet (57). However, this study had a slightly different definition for the outcome (coronary artery disease) and used different methods. WHO 2020 data shows that CHD mortality reaches 12.26% in Nepal (58).

Despite the use of self-reported data, our study found a prevalence of angina at 3.42%, whereas a similar urban study done in Nepal in Dharan municipality found the prevalence of angina to be 3.60%. Our study uses standardized RAQ questions based on self-reported data whereas the Dharan study used the Minnesota codes for interpreting positive Rose angina questionnaire. Similar to this, other studies found that a prevalence of 3.50 % measured in a cohort of 28,000 participants using the RAQ method categorized angina based on angina or no angina (23). Another study found the prevalence of angina at 6.9% using the locally validated rose angina questionnaire, rose positive angina was interpreted using Minnesota codes (25). Our study employs a method similar to that used in India, which involves a Rose Angina Questionnaire (RAQ) with seven questions. In this approach, a positive self-reported response indicates angina, while a negative response indicates no angina. In the Indian study, the prevalence of angina was 4.69% in males and 7.02% in females (32).

Many studies have shown that prevalent angina is lower in males than females. A cross-sectional Whitehall II study shows females are more likely to develop angina, with a prevalence of 4.0 % while the prevalence for males is found to be 2.4% (31) Similar result to the Indian study where they used self-reported RAQ questionnaire found prevalent of angina in male to be 4.69% and 7.02% in women.(32) Angina was most common in women, and heart disease was common in

men. This result was very similar to our study where the prevalence of men was found to be 2.60% and female higher than men, 3.98%. Our studies found no association of angina between angina and gender in unadjusted models and adjusting socio-demographics. However, after adjusting all risk factors, we found a reduced risk of angina for males (OR: 0.52, 95% CI: 0.25–1.10, p 0.09) whereas previous study shows association with female (OR: 0.61, 95% CI: 0.43- 0.85) (32). This agrees that men have a lower risk of developing angina in these studies. A potential reason may be that, also women in some cultures present with heart symptoms differently than men, which might not always be captured effectively by the RAQ. In addition, women in our study had a higher prevalence of obesity, and this may have contributed to their increased risk for angina. However, other risk factors, such as smoking and drinking have been historically more prevalent among men, which contributes to an increase in heart disease. Additional research is needed to understand these gender differences better.

**Angina associated with other co- variates:** Numerous studies have shown that increasing age and higher BMI are associated with an elevated risk of developing angina. Higher age is a risk factor for angina (32) (31) (26). There is an association of BMI with angina, higher risk of having angina with overweight participants (OR: 3.05, 95% CI: 1.48- 6.29), obese (a OR: 4.92, 95% CI: 2.18- 11.09) in our study. Our study agreed with these findings.

Education shows a significant association with angina. An Indian study shows (OR: 1.32, 95% CI: 0.96 – 1.82) for those who have lower education (32) , another study shows with less education (OR: 1.41, 95% CI: 1.10 -1.79) shows people with lower education than high school were likely to have angina (23). Our results differed for participants whose education was less than high school (OR: 0.15, 95% CI: 0.20–1.20, p-value 0.07). A significant increased association was found with those having no formal education but only in the unadjusted model (OR: 0.07, 95% CI: 1.18- 3.62,

p= 0.01). Adjustment of other related factors may have impacted the adjusted model. Regardless, our finding of the increased association with angina in those with no formal education agrees with others, reflecting that these participants may be unaware of health hazards resulting in poorer health outcomes (23). The J- shaped association showing those with some education having lower risk that higher educated participants may be related to the recent epidemiologic transition in Nepal as the nation's economic status changed from a low to a middle income country (44). It is possible that confounding by higher income, providing access to more Western foods, less physical exercise in office jobs, or other related factors may be influencing this finding.

Other co- variates include association of angina with hypertension (OR: 1.54, 95% CI: 1.14 – 2.09), smoking (OR: 0.67, 95% CI: 0.43- 1.03) in self-reported RAQ questionnaire in Indian studies (32) which differ from the Nepalese study. Our study shows an increased risk of angina associated with hypertension only in men (OR: 4.66, 95% CI: 1.50-14.40, p=0.008) and higher risk of angina with former smoker (OR: 4.17, 95% CI: 1.98- 8.76). This may be because of their larger sample size, or other confounding factors, as discussed above.

Although we found an increased association between angina and hypertension in men, many other studies have shown increases due to both hypertension and diabetes. The lack of association in females may be due to our study's low number of smokers. Regarding diabetes, although the trend suggests it could influence angina risk, our study did not have sufficient statistical power to establish a significant effect.

The prevalence of CHD was found to be 7.65% in our study which is comparatively higher than another study done in eastern Nepal, which shows a prevalence of 5.7% among the male population aged greater or equal to 35 years of age. (26) This difference may be due to the inclusion of both genders in our study, whereas other Nepali study was only done within the risk age group

population with only male participants. Similar to the method used in our study, another Lebanese study shows CHD prevalent at 13.4% among the age group greater than 40 years of age (34). Similarly, a Sri Lankan study shows CHD prevalence to be 6.4% using a validated tool (25). These contrasts are more likely due to differences in study methodologies and demographic variations.

An Indian study shows the prevalence of CHD found to be 31.9% per 1000 in the age group 25-64 years based on hospital records, or ECG evidence by Minnesota code (59) This is different than the methods we used in our study. Our study is entirely self-reported and does not rely on the findings of clinical records. Another study conducted in Iran found the prevalence of CHD to be 9.2% with a self-developed questionnaire, not with the validated RAQ (35).

**CHD associated with gender and education:** Many studies done globally show that CHD prevalence is associated with greater age and with more males than females (59), (35), (34). Males are more vulnerable to having CHD than females. Results for the Indian study shows CHD associated with 39.5% in men and 25.3% in females (59), similarly greater in males (OR =2.25, 95% CI =1.62–3.13) in Lebanese study (34). Similarly, that study also shows that the prevalence of CHD was higher in those with lower levels of education (OR: 1.67, 95% CI: 1.21- 2.30) (34). Our study indicates a reduced risk of angina associated with lower education levels, with participants having less than a high school education showing an odds ratio (OR) of 0.39 (95% CI: 0.18–0.81). These results differ from another study conducted in Nepal, which found an odds ratio of 1.52 (95% CI: 0.38–6.14), in which the direction of the association differs (26). Our study shows an association with a decreased likelihood of having CHD for participants with less education below high school level (OR: 0.39, 95% CI: 0.18- 0.81, p-value 0.01) and males higher than females (OR: 0.53, 95% CI: 0.32- 0.86, p-value 0.01).

Different studies show that CHD is associated with other co- variates including smoking, BMI and diet. A Lebanese study that uses a similar methodology as ours shows a strong association with hypertension (OR: 2.64, 95% CI: 1.36 – 5.11) and diabetes (OR: 5.20, 95% CI: 2.97- 9.07) (34). Similar result with the Iran study where they elucidate association with diabetes (OR: 1.28, 95% CI: 1.08- 1.51), hypertension (OR: 2.23, 95% CI: 1.92- 2.60) (35). Our study may not have been sufficiently powered to show these associations. In contrast, our study found that overweight to be higher at 34.51%, obesity was 15.61%, current smoking was 16.92%, current drinking was 14.43%, and hypertension was 36.07%. This may be due to differences in data collection and definitions of the study variables.

In our study, CHD associated by BMI overweight (OR: 1.69, 95% CI: 1.07- 2.65, p-value 0.02), obesity (OR: 1.90, 95% CI: 1.09- 3.28, p 0.02) and former smokers (OR: 2.35, 95% CI: 1.30- 4.25, p 0.004), and unhealthy diet (OR: 0.52, 95% CI: 0.33- 0.83, p 0.006). Despite the differences in different studies using self-reported and clinical experiences with validated RAQ questionnaire, our study shares some similarities in association with co-variates, including high BMI, smoking, and low physical activity.

### **Strengths of this study**

A major strength of this study relies upon the standardized data collection and quality control utilized in the DHS. It is the largest cardiovascular disease study in Nepal, with a sample of 1608. The study was comprehensive in its ability to gather both self- reported information on behavioral risk factors as well as medical history (e.g., smoking behaviors, alcohol behavior, calculation of body mass index, diet pattern, physical activity). In- person measurements were made to collect

BMI and blood pressure. This study is helpful to generate public health policies and develop interventions to reduce cardiovascular disease burden in a low- to middle-income country, Nepal.

### **Limitations of this study**

Every cross-sectional study has its own limitations. Using this secondary dataset, we were not able to generate data outside of those selected by the DHS. In addition, it is not possible to determine the temporality of variables. The prevalence of angina was found to be low (3.42%), although it is unclear if this is due to the self-reported aspect of the RAQ and perhaps lack of clarity in the definition. A comparison with physician- determined angina would be interesting. It is also possible that misclassified data occurred due to response bias that arises when people answer some questions based on attitudes, experiences, or personal beliefs, or because they answered as they believed the interviewer expected. We cannot generalize our findings to the overall Nepalese population as BMI, diet, and lifestyle factors may differ from one region to another. Our study might also not apply to other South Asian countries as Nepal has a diverse cultural, genetic, and diet preferences, which may be unique regarding countries outside Nepal.

### **Conclusions**

This study is one of few reporting on risk factors for angina and CHD in Nepal. Our results confirmed many associations found in the other comparable Nepalese studies. We also found trends similar to other studies conducted in South Asian countries showing results for risk factors including age, behavioral factors like smoking, physical activity, and alcohol intake. For socio-demographic characteristics, age is a major variable to elucidate associations with angina and CHD and was found to increase risk across all studies.

The implications of this study include the need for targeted interventions and policy measures to address risk factors and provide policies, programs, and behavioral change initiatives at the local, community, and governmental levels. In addition, there is an increasing need for community-based programs to increase public awareness of cardiovascular disease and its risk factors, as well as to collaborate with international non-governmental organizations (INGOs), government agencies, healthcare providers, and schools to improve community participation and social awareness. A national strategy to control the prevalence of cardiovascular disease, including angina pectoris and CHD is needed. Implementing public health initiatives and programs can be aided by identifying risk factors for CHD and angina. To reduce the risks of CVD in urban environments, the results of this study can be utilized to create guidelines for CVD risk factors such as alcohol consumption, smoking, diabetes awareness, and hypertension. Additionally, dietary and behavioral interventions can be carried out. This will aid in preventing cardiovascular disease by strengthening the health system and exploring the boundaries to conduct further research and investigations on CVDs.

**Author Disclosure Statement:**

No Conflicts of interest or competing financial interests are declared.

**Attribution of Support:**

“This research project and my MPH Studies were supported by the Cardiometabolic Research and Training Program (CMRTP) through *Building Capacity to Address the Burden of Cardiometabolic Risk Factors and Diseases in LMICs*, a grant from the US National Institutes of Health Fogarty International Center (FIC) D43 TW011596.”

**Contributors/ Footnotes:**

I would like to extend my heartfelt thanks to my thesis chair, Dr. Annette L. Fitzpatrick, PhD, and my committee members, Dr. Sarah Masyuko, PhD, and Dr. Archana Shrestha, PhD, for their invaluable guidance, unwavering support, and timely supervision throughout this process. A big gratitude to all the members of the CMRTP/ IARTP teams for their continuous support and for helping me stay on track. This project would not have been completed without their assistance. I also wish to express my sincere thanks to the University of Washington's Department of Global Health, Kathmandu University School of Public Health, and Dhulikhel Hospital for involving me in this research project and contributing to its success.

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## Appendix

### Questionnaire 1. Original DHS Rose Angina Questionnaire (14)

#### Rose Angina

1. Within the last one year, have you ever had a severe pain across the front of your chest lasting for half an hour.  
or more? (a) Yes \_\_\_ (b) No \_\_\_
2. Did the pain occur for the first time in the last year? (a) Yes \_\_\_ (b) No \_\_\_
3. Within the last one year, have you ever had a pain or discomfort in your chest? (a) Yes \_\_\_  
(b) No \_\_\_
4. If no on previous question, within the last one year, have you ever had any pressure or heaviness in your chest?  
(a) Yes \_\_\_ (b) No \_\_\_
5. Did the pain/discomfort/pressure/heaviness in the chest occur for the first time in the last year?  
(a) Yes \_\_\_  
(b) No \_\_\_
6. Do you get it when you walk uphill or hurry? (a) Yes \_\_\_ (b) No \_\_\_
7. Do you get it when you walk at an ordinary pace on the level? (a) Yes \_\_\_ (b) No \_\_\_
8. What do you do if you get it while you are walking? (Probe) \_\_\_\_\_
9. If you stand still, what happens to it? (Probe) \_\_\_\_\_
10. Where do you get this pain or discomfort? (Write the code of the region)  
(a) A \_\_\_ (b) B \_\_\_ (c) C \_\_\_ (d) D \_\_\_ (e) E \_\_\_  
(f) F \_\_\_
11. You said you had severe pain in across the front of your chest lasting for half an hour or more, did you see a  
12. doctor because of this pain? (a) Yes \_\_\_ (b) No \_\_\_
13. If you saw a doctor, what did your doctor say it was? (a) Angina \_\_\_ (b)  
Heart attack \_\_\_ (c) Don't know \_\_\_  
(d) Other \_\_\_
14. If Other on previous question, please specify: \_\_\_\_\_
15. How soon is it relieved? (a) \_\_\_ (b) \_