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Research Article

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Coronary Artery Disease Risk Factors among Females in a Tertiary Cardiac Centre in Nepal: A Case Control Study

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Abstract

Background: Although in recent decades risk factors of Coronary Artery Disease (CAD) have markedly increased, little is known about its relationship among Asian females. The principal aim of the study is to determine the prevalence of CAD risk factors among a target female population in Nepal.

Methods: A case control study was conducted at tertiary cardiac centre of Kathmandu from August 2013 to September 2014. Study participants identified with CAD (n=52) were matched for age with controls (n=52). Anthropometric and laboratory data were collected and a semi-structured interview was utilized to obtain information on socio-demographic, behavioural, psychosocial and physiological/biochemical risk factors. Variables were assessed using frequency tables and Pearson's Chi-Square tests for two independent proportions. Binary logistic regression was used to investigate the potential predictors of CAD.

Results: CAD was significantly associated with ethnicity, ever smoked, harmful use of alcohol, moderate physical activity, more than 12 sitting hours per day, family history, total cholesterol, HDL-C and hypertension. Regression analysis indicated alcohol intake (P<0.01), LDL-C, diabetes (P<0.01), BMI ≥ 27.5 kg/m^2 (P<0.01) as significant predictors of CAD.

Conclusion: Diabetes, drinking alcohol, LDL-C and generalized obesity were found to be significant predictors of CAD. Aside from family history, all associated risk factors within our study population are modifiable risk factors. CAD has been identified as public health priority in Nepal given the current and predicted burden of all forms of heart disease within the country. Further research in women in developing countries will be key, given the rising levels of risk factors and morbidity rates within the region.

Keywords

Coronary artery disease; Females; Non communicable diseases; Risk factors; Nepal

Background

Cardiovascular disease (CVD), the leading cause of death worldwide, kills 17 million people each year which represents 30% of all global deaths [1]. In Nepal, CVD accounts for 22% of all deaths placing it as the number one cause of death and CAD, a form of CVD, has surpassed infectious diseases as the leading cause of mortality within the country [2]. CAD mortality has been shown to be higher in women than in men [3], indicating that up to 40% of all coronary events in women may be fatal [4]. In developing countries like Nepal where the required medical and surgical interventions for CAD are inaccessible to the majority of the population, disease prevention and health promotion strategies are critical. Early identification of risk factors in both men and women will be vital in curbing the growing CAD epidemic.

Gender specific differences regarding etiology, pathophysiology, symptoms, diagnosis, therapy and prognosis of CAD have previously been identified [5]. Although women are principally subject to the same atherogenic risk factors as men, the importance and relative weighing of these factors are different. Hence, identifying the significance of key CAD risk factors in women holds important implication for both prevention and treatment. The aim of this study was therefore to determine the prevalence of CAD risk factors among a target female population in Nepal.

Methods

Study populations

A case control research design was adopted. The study was conducted in the Sahid Gangalal National Heart Centre (SGNHC), a tertiary cardiac centre in Kathmandu, Nepal from August 2013 to September 2014. Purposive sampling was used for the selection of cases and controls. Cases were selected from outpatient departments (OPD) and inpatient wards of the SGNHC and included female patients aged ≥ 25 to ≤ 75 years, with the diagnosis of CAD. For each case, one age matched control was selected. Age matching was done with the liability of ± 1 years of age. Age matched controls were defined as visitors with non-cardiac complaints at the same hospital during the same period of time. With the reference study among Pakistani females, the sample size was calculated as 104, 52 in each case and control group, using the formula [6].

$$n=(Z_{1-\alpha/2}+Z_{1-\beta})^2\, pq\, (r+1)/(P_1-P_2)^2\, r$$

Exclusion criteria for both cases and controls included subjects previously diagnosed with renal disease, neurological disease or other mental health related disease.

Definitions

The diagnosis of CAD was made by a cardiologist on the basis of both clinical symptoms and further testing including; electrocardiogram (ECG) abnormalities, cardiac enzymes and/or echocardiography. Women who had stopped smoking for a year or more were considered former smokers. Patients with a history of CAD in first degree male relatives of ≤ 55 years or in female relatives less than ≤ 65 years were regarded as having a positive family history of premature CAD. Patients taking oral hypoglycemic drugs, insulin or those having random blood sugar of more than 200 mg/dl were regarded as having diabetes mellitus. Females taking antihypertensive drugs or whose systolic pressure was above 140 mm Hg or diastolic blood

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pressure above 90 mm Hg taken on two subsequent measurements in sitting position were considered as having hypertension. Serum lipid reference levels criteria using the National Cholesterol Education Programme (NCEP) Adult Treatment Panel III (ATP III) guideline define hypercholesterolemia as total cholesterol>200 mg/dl, high LDL-C>100 mg/dl, hypertriglyceridemia as TG>150 mg/dl and low HDL-C<40 mg/dl [7]. Dyslipidemia was defined by the presence of one or more abnormal serum lipid concentration measurement [8]. Females with a body mass index (BMI) ≥ 27.5 kg/m^2 were considered as obese. Females with a waist to hip ratio greater than 0.81 were considered as having central obesity [9].

Research instrument

A semi-structured interview was developed consisting of socio-demographic, behavioural, psychosocial, biochemical and physiological factors. Ethnicity of cases was classified into four groups based on the Health Management Information System, Department of Health Services, Ministry of Health and Population [10]. Socio-economic status (SES) was assessed using a modified Kuppuswamy scale for Nepal where SES is categorized into lower, middle and upper [11]. Alcohol intake was not type specific and was determined as any use of alcohol in the past year. The CAGE substance abuse screening tool was used to assess harmful use of alcohol. The tool consisted of four questions scored as either 0 or 1. A total score of 2 or greater was considered clinically significant [12]. Physical activity was measured using the IPAQ (International Physical Activity Questionnaires) [13] and a perceived stress scale was used to assess the degree of stress [14]. The perceived stress scale consisted of ten questions, each rated into five domains: almost never (AN), never (N), sometimes (S), fairly often (FO) and very often (VO). Additional questions were developed as per the objectives of the study based on an initial desktop review and expert opinion. The research instrument was pretested among ten samples (10% of the total sample size) in the medical ward and coronary care unit (CCU) at B.P. Koirala Institute of Health Sciences (BPKIHS), the tertiary hospital of the eastern region of Nepal but no modifications were required.

Ethical consideration

The research proposal was approved by the institutional ethical review board (IERB) of BPKIHS. Permission to conduct the study was obtained from the SGNHC administration as well as from Matron, Nursing Officers and Cardiologists. Individual participant written consent was obtained from all participants.

Data collection procedure

Structured questionnaires were conducted among predefined CAD cases selected from both OPD and inpatient wards. Identical questionnaires were used among controls selected from OPDs of the same centre. Height, weight and waist circumference were measured in both groups using standardized techniques and equipment. The reference point used to measure waist circumference with a non-stretchable tape was regarded as the highest point of the iliac crest. The narrowest region (visible waist) of the abdomen was used when this region did not coincide with the highest point of the iliac crest.

Blood pressure was measured with a sphygmomanometer and stethoscope at least twice in each participant with at least 5 min of rest in between, with the subject seated in a chair and relaxed, the back supported, and the arm at heart level.

Blood sample was taken for the blood glucose and lipid profile. Hospital charts were also used to obtain clinical reports of CAD diagnosis. Subjects and local administration were asked for permission before obtaining information from patient charts. Blood glucose was determined using capillary blood obtained from a pin prick on finger pulp measured by a calibrated glucometer. Outpatient participants were escorted to the SGNHC laboratory where a blood sample for lipid profile was drawn by a professional.

Statistical analysis

The collected data were entered into SPSS V20.0 for Windows (IBM SPSS Inc, Chicago, Illinois, USA). The distribution of the variables was assessed using frequency tables and Pearson's Chi-Square tests for two independent proportions. A p value ≤ 0.05 was considered as statistically significant. Binary logistic regression was used to investigate the potential predictors of CAD.

Results

CAD presented as myocardial infarction in half of cases (50%), followed by angina pectoris (19.2%), double vessel disease (DVD)/ triple vessel disease (TVD) (15.3%), arrhythmias (11.5%) and heart failure (3.8%).The mean age of respondents was 56.38 ± 11.55 years. Most (82.7%) respondents in both case and control group were married. On the basis of modified Kuppuswamy SES scale for Nepal, 50% of cases and 67.3% of controls belonged to middle SES (Table 1).

The relationship of CAD with baseline socio-demographic characteristics is shown in Table 1. A significant association was found with ethnicity and a positive family history of CAD. Similarly, using Pearson Chi-Square test, behavioural, physiological and biochemical risk factors as well as perceived stress level were analyzed and are shown in Tables 2 and 3. Smoking status, alcohol intake, harmful use of alcohol, moderate physical activity, sitting more than 12 h, perceived stress level, total cholesterol, LDL-C, HDL-C, diabetes, hypertension and generalized obesity were all associated with CAD. The cumulative effects of significantly associated risk factors are shown in Table 4. Binary logistic regression revealed alcohol intake, LDL-C, diabetes and generalized obesity as significant predictors of CAD.

Discussion

In our study, we demonstrate that the majority of cases belonged to relatively advantaged janajatis which reflects findings from previous studies in Nepal [10]. Higher SES has been shown to increase the prevalence of hypercholesterolemia, hypertriglyceridemia and sedentary life style consequently increasing the prevalence of CAD [15]. However, the bulk of our cases belonged to middle SES subjects, allthogh no significant association was found in relation to CAD. Family history as a risk factor of CAD in our population is consistent with previous work conducted in similar Asian populations in Pakistani women as well as other western female populations [16,17]. Three fourth of cases were in post-menopausal compared to 60% of controls however; there was no significant association with CAD in contrast to previous work conducted among Nepalese women [18]. Regarding the use of OCPs, our results concur with previous meta-analysis which illustrates no difference between the overall risks of cardiovascular events in OCPs users [19]. Although hysterectomy has been suggested as a possible risk factor for CAD [20] our findings did not indicate an association between the two.

Having ever smoked was associated with CAD in our population, consistent with previous studies indicating smoking as an important atherogenic risk factor leading to CVD [21]. Current smokers were

Table 1: Baseline socio-demographic characteristics of cases and controls.

Variables	Category	Cases (n=52)%	Controls (n=52)%	OR (95% CI)	p value
Age	Less than 45 years	19.2	19.2	NA	1.0
	45-55 yrs	25	25		
	56-65 yrs	32.7	32.7		
	More than 65 yrs	23.1	23.1		
Marital status	Single	25	17.3	1.6 (0.6-4.1)	0.337
	Married	75	82.7		
Ethnicity	Upper Caste	32.7	57.7	Reference	**0.025**
	Disadvantaged janajati	15.4	17.3	0.6 (0.2-1.9)	
	Relatively advantaged janajati	36.5	21.2	0.3 (0.0-1.8)	
	Others*	15.4	3.8	0.1 (0.0-0.7)	
Education	Illiterate	63.5	42.3	Reference	0.149
	Primary school/Literate	9.6	21.2	3.3 (1.0-11.0)	
	Middle/High School Certificate	15.4	23.1	2.2 (0.8-6.4)	
	Intermediate and above	11.5	13.5	1.7 (0.5-6.0)	
Occupation	Unemployed	48.1	30.8	Reference	0.270
	Clerical/Shop owner/Farmer	26.9	28.8	1.7 (0.6-4.4)	
	Profession/Semi-profession	13.5	23.1	2.7 (0.9-8.2)	
	Others	11.5	17.3	2.3 (0.7-7.9)	
Family income	NPR ≤ 22850 per month	48.1	38.5	1.5 (0.7- 3.2)	0.322
	NPR>22850per month	51.9	61.5		
Socio-economic status	Upper	11.5	11.5	Reference	0.139
	Middle	50	67.3	1.3 (0.4-4.7)	
	Lower	38.5	21.2	0.5 (1.4-2.1)	

NPR: Nepalese Rupee

*Others include dalit, disadvantaged non dalit janati and religious minorities

Table 2: Association of risk factors and perceived stress levels with coronary artery disease.

Characteristics	Categories	Case (n=52) %	Control (n=52) %	OR (95% CI)	P value
Ever smoke	Yes	42.3	11.5	5.6 (2.0-15.5)	**<0.001**
	No	57.7	88.5		
If yes,	Current	42.9	42.9	1.0 (0.2-4.5)	1.000
	Former	57.1	57.1		
Alcohol intake	Yes	48.1	21.2	3.5 (1.5-8.1)	**0.004**
	No	51.9	78.8		
Harmful use of alcohol	Yes	68	90.9	21.3 (2.3-195.8)	**0.001**
	No	32	9.1		
Diet type	Vegetarian	15.4	26.9	2.0 (0.8-5.3)	0.15
	Non-vegetarian	84.6	73.1		
Cooking method	Ghee (butter)	5.8	1.9	Reference	0.051
	Mustard oil	32.7	15.4	1.4 (0.1-15.8)	
	Refined oil	61.5	82.7	4.0 (0.4-40.5)	
Vigorous physical activity	Yes	13.5	21.2	0.6 (0.2-1.6)	0.300
	No	86.5	78.8		
Moderate physical activity	Yes	38.5	63.5	0.4 (0.2-0.8)	**0.011**
	No	61.5	36.5		
Sitting hours	More than 12 hours	67.3	40.4	3.0 (1.4-6.8)	**0.006**
	Less than 12 hours	32.7	59.6		
Perceived stress level	More than average	90.4	34.6	17.8 (6.0-52.5)	**<0.001**
	Less or equal to average	9.6	65.4		
Family history of CAD	Yes	34.6	9.6	5.0 (1.7-14.8)	**0.002**
	No	65.4	90.4		
If yes,	Parental Sibbling	88.8 11.1	50 50		

Menopause	Yes	73.1	59.6	1.9 (0.8-4.2)	0.146
	No	26.9	40.4		
Oral contraceptive pills	Yes	13.5	7.7	1.9 (0.5-6.8)	0.339
	No	86.5	92.3		
Hysterectomy	Yes	13.5	11.5	1.2 (0.4-3.8)	0.767
	No	86.5	88.5		

CAD: Coronary Artery Disease

Table 3: Association of metabolic risk factors with coronary artery disease.

Characteristics	Category	Case (n=52)	Control (n=52)	OR (95% CI)	P values
		%	%		
Total Cholesterol	≤ 200 mg/dl	53.8	75	2.8 (1.1-,6.0)	**0.024**
	>200mg/dl	46.2	25		
LDL-C	≤ 100 mg/dl	44.2	75	3.8 (1.6-8.7)	**0.001**
	>100 mg/dl	55.8	25		
HDL-C	<40 mg/dl	61.5	30.8	3.6 (1.6-8.1)	**0.002**
	≥ 40 mg/dl	38.5	69.2		
Triglycerides	≤ 150 mg/dl	57.7	44.2	0.6 (0.3-1.3)	0.170
	>150 mg/dl	42.3	55.8		
Diabetes	Yes	48.1	15.4	5.1 (2.0-12.9)	**<0.001**
	No	51.9	84.6		
Hypertension	Yes	69.2	48.1	2.4 (1.1-5.4)	**0.029**
	No	30.8	51.9		
BMI	≥ 27.5 kg/m^2	32.7	59.6	3.0 (1.4-6.8)	**0.006**
	<27.5 kg/m^2	67.3	40.4		
Waist Hip Ratio	>0.81	84.6	92.3	0.4 (0.1-1.7)	0.220
	≤ 0.81	15.3	7.7		

LDL-C: Low-Density Lipoprotein Cholesterol; HDL-C: High Density Lipoprotein Cholesterol; BMI: Body Mass Index

Table 4: Logistic regression results for the association of risk factors with coronary artery disease.

Variables	Beta value	Standard Error	Wald	df (degree of freedom)	p value	OR (95% CI)
Alcohol intake	-1.294	0.571	5.137	1	**0.023**	3.7 (1.2-11.2)
Moderate physical activities	0.349	0.565	0.382	1	0.536	1.4 (0.5-4.3)
Sitting hours	-0.706	0.576	1.504	1	0.220	2.0 (0.6-6.3)
Total Cholesterol	0.416	0.618	0.452	1	0.501	0.7 (0.2-2.2)
LDL-C	-1.964	0.662	8.799	1	**0.003**	7.1 (2.0-26.1)
HDL-C	-0.351	0.555	0.400	1	0.527	1.4 (0.5-4.2)
Diabetes	-1.649	0.629	6.867	1	**0.009**	5.2 (1.5-17.9)
Hypertension	-0.415	0.517	0.642	1	0.423	1.5 (0.5-4.2)
BMI ≥ 27.5 kg/m^2	1.463	0.526	7.738	1	**0.005**	4.3 (1.5-12.1)

not associated with higher levels of CAD, most likely due to the small proportion of current smokers within the study population, totalling only 6 (11.5%). Harmful use of alcohol presented a strong association with CAD (OR 3.5 [2.3-195.8]) consistent with previous study [7] however; the small sample size within the control group did not permit for further logistical regression analysis.

Physical activity decreases resting blood pressure, increases serum HDL cholesterol and decreases triglycerides independently of any weight loss [22] yet in our study, there was no association of CAD with vigorous physical activity although those engaged in moderate physical activity and less than 12 sitting hours did show a lower association with CAD. This is consistent with findings from the 2004 INTERHEART study, demonstrating the protective effect of exercise, where it was found to be especially greater in women compared to men [17]. Females who perceive higher stress level presented with a higher association of CAD, similar to previous findings signalling that subjects with higher perceived stress levels are 18 times more likely of developing CAD [23].

The present findings associating total cholesterol, LDL-C and HDL-C to CAD are similar to previous studies from the National Heart, Lung and Blood Institute (NHLBI), seven countries study, and Framingham [15,24]. Close to 70 percent of cases and almost halve of controls had previously diagnosed hypertension which is far greater than the national average of 24.1 percent [25] likely due to the fact that the study was conducted in a hospital setting. The present study findings are consistent with previous work conducted by Yalc et al. [26] and Moreira et al. [27] demonstrating a significant relationship between hypertension and CAD among females. Similarly, our study population demonstrated an association between overweight and obesity and CAD [17,26]. No significant association was found among CAD and centralized obesity, documented in other studies [6].

Study strengths and limitations

Although CAD associated mortality rates in women in low-and middle-income countries (LMIC) are higher than in industrialized

nations, the bulk of evidence describing causal links between risk factors and disease is still generated from industrialized nations [15]. This study provides insights as to key risk factors leading to CAD amongst women in Nepal, a LMIC. Moreover, it explores elements such as SES, physical activity levels, sedentarism, perceived stress levels and alcohol abuse that are not regularly considered within clinical practice in Nepal. Nevertheless, our study does present some methodological limitations that must be considered in interpreting the present findings. First, our small sample size may have not made it possible to detect all associations among surveyed risk factors. Secondly, not all associated risk factors obtained from bivariate analysis were incorporated into logistic regression analysis due to small sample size after stratification. Additionally, our study population might not reflect the generalized population of Nepal given that both cases and controls were recruited from a hospital setting.

Conclusion

Misperceptions regarding CAD as not a real problem for women still exist in Nepal. In western societies it is estimated that 1 in 2 women will die of heart disease or stroke, compared to 1 in 25 who will eventually die of breast cancer [28]. The current study demonstrated twelve risk factors among which alcohol intake, LDL-C, diabetes and generalized obesity were found as significant predictors of CAD. Apart from family history, all associated risk factors within our study population are modifiable risk factors. CAD in women will remain a public health priority as substantial numbers of aging women will become at greater risk for all forms of CVD in Nepal. Further research in women in developing countries will be key, given the rising levels of risk factors and morbidity rates in these populations. Similar to many societies around the world, Nepalese women play a crucial role within the family structure in terms of feeding, educating and caring for family members. Educating women greatly increases willingness and ability to take heart-protective action not only for them but for their families. Thus, policy makers and health care systems in general should regard women as critical agents of change for the control and prevention of CVD.

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