Original Article

Analysis of traditional risk factors for ischemic heart disease in Nepalese females with anginal chest pain

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Abstract

Background: Ischemic heart disease has emerged as one of the important causes of deaths in females in most of the countries. IHD is killing women more significantly in recent years. Females with anginal chest pain are often treated differently as compared to males at the time of presentation. In Nepalese female population, the burden and impact of traditional risk factors for IHD have been less studied.

Methods: It was a single centre , hospital based, case control, descriptive study comprising of 155 female patients with angina in case arm and 155 otherwise healthy females in control arm. The study period was of one year duration. Cases and controls were matched in a 1:1 frequency matching manner with respect to age. Written consents were taken. Data were collected after complete history taking, physical examination, laboratory investigations. Subsequently statistical analysis was done. First bivariate analysis followed by multivariate analysis were done using latest version of SPSS in regards to comparison of risk factors between two groups.

Results: The average age of cases was 60.50 ± 11.13 years and 60.37 ± 10.68 years for controls. The most prevalent risk factor of IHD in cases and control was HTN (53.3% vs 40%). The statistically significant risk factors for IHD that were found in females with angina were - Smoking (AOR=3.190, 95% CI:1.606, 6.334 and p=0.001), Diabetes (AOR=2.573, 95% CI: 1.346, 4.918 and p=0.004) , and Obesity/overweight (AOR=2.482, 95% CI: 1.475, 4.176 and p=0.001).

Conclusion: The important risk factors for IHD that are associated significantly with likelihood of having angina in Nepalese females are smoking, diabetes and overweight/obesity in our study.

Introduction

In recent years, the coronary death rate among young adults irrespective of sex, is rising, however the increase is more prominent among young females.[1] This is more likely to be due to steady increases in unfavorable risk factors for IHD, especially DM, HTN and metabolic syndrome.[2,3]

Certain risk factors are more causally related to IHD in females, which include DM, metabolic syndrome, low HDL-C and smoking.3[4,5,6]

Diabetes increases the risk for CAD among women by 3–7 times, versus 2–3 times increased risk in diabetic men.[4]

Likewise, smoking has been found to be more deleterious to women. Female smokers die 14.5 years earlier (versus female nonsmokers).[6]

In the Framingham study, low HDL-C was found to be a predictor of CAD, more so in women than men.[7]

Elevated triglycerides have been shown to be of greater risk to women than to the male counterparts.[8,9,10]

In contrast to the linear increase in CAD in men as they age, there is a more exponential increase in CAD in women after the age of 60 years.[11]

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The clinical diagnosis of chest pain in females is a difficult task. Generally, the age at presentation for females is 10 years later, compared to males. Females present less with typical angina and present more with atypical angina and noncoronary chest pain syndromes.[12,13]

These differences must be taken into consideration while evaluating chest pain in females. As the clinical manifestations of IHD are so vague in females, some noninvasive investigations may be needed to rule out IHD. The urbanization and changing lifestyle and dietery patterns have produced more pronounced detrimental effects in occurrence of IHD via establishment of more number of traditional risk factors in Nepalese female population. One of the most common presentations of IHD in females is angina. The rising pattern of morbidity and mortality due to IHD in Nepalese females is not well studied. We aim to find out which traditional risk factors for IHD are more strongly associated with Nepalese female patients presenting with anginal chest pain.

Methods

It was a single centre, hospital based, case control, descriptive study comprising of 155 female patients with angina in case arm and 155 otherwise healthy females in control arm. The study period was of one year duration. It was started on 16th march 2023 and completed on 15th march 2024. This study was carried out at the Department of Internal medicine of Pokhara Academy of Health Sciences (POAHS), which is one of the leading referral tertiary care centers of Nepal. Cases and controls were matched in a 1:1 frequency matching manner with respect to age.

Sample size was calculated by the formula :

$$N=((z\alpha\sqrt{(2p(1-p))} + z_{\beta}\sqrt{(p1(1-p1)+p2(1-p2))/(p1-p2))^2},$$

where zα=1.96 at 95% confidence interval and z_{β}=0.84 at 80% power,

P1=0.32 (prevalence of most significant risk factor (DM) in females with IHD in Nepal= 32%).[14,15]

P2=0.183 (prevalence of the most significant risk factor for IHD in normal female population of Nepal =18.3%).[16]

P=(p1+p2)/2, So the sample size came out to be about , N=155 for each case and control group.

Inclusion criteria for cases:

1) All female cases with anginal chest pain.
2) Age >16 years and < 85 years.

Exclusion criteria for cases:

1) Patients without consent.
2) Patients who are suffering from chronic kidney disease, valvular heart disease, cardiomyopathy, pulmonary arterial hypertension, congenital heart disease, pregnancy.
3) Patients having noncardiac causes of chest pain such as infection and trauma.
4) Patients with unstable medical disorders that affect patients safety and successful participation in the study for example, cases under mechanical ventilation, with active malignancy.

Inclusion criteria for controls:

In control arm, age matched females who are apparently healthy without history of angina and who came for general health checkup in medicine/cardiology OPD were enrolled.

Exclusion criteria for controls:

1. History of diagnosed IHD, CKD, VHD, cardiomyopathy, PAH, congenital heart disease in the past.
2. Non cardiac causes of chest pain.
3. Unstable medical and psychiatry disorders.
4. Unwilling to give consent.

Data collection from patients included in the study was done using the following tools:

1. Questionnaires
2. Physical examination
3. Laboratory investigations

Definitions:

The classification of angina : typical or atypical.

Typical angina if all of the following criteria were met:

1. substernal chest pain described as a feeling of heaviness,squeezing, crushing, or tightness,
2. provoked by exertion or emotional stress, and
3. relieved by rest and/or nitroglycerine within minutes.

If two of the criteria were present, the pain was atypical angina. If one or none of the criteria was present, the pain was considered as noncardiac chest pain.[17]

Dyslipidemia was defined as the presence of any of the following: patients on lipid lowering drugs or total cholesterol >240 mg/dl, triglycerides (TG) >150 mg/dl, low-density lipoprotein >130 mg/dl, and high-density lipoproteins (HDL) <50 mg/dl.[18]

Positive family history of CAD was defined if the first degree relatives suffered from CAD before the age of 65 years in women.[19]

Diabetes Mellitus was defined as symptoms of diabetes, fasting blood sugar >126 mg/ dl (7.0 mmol/L) or HbA1C level > 6.5 or if patient was on oral hypoglycemic agents according ADA guidelines.[20]

Hypertension was defined as systolic blood pressure >140 and/ or diastolic >90 mmHg and/or on anti-hypertensive treatment according to JNC-8 guidelines.[21]

Obesity was defined according to Asian-indian consensus guidelines.[22]

Physical activity or exercise for <150 min/week was taken as the criteria for defining sedentary life style.[23]

Statistical Analysis

Data were documented in an excel sheet and then analyzed using the latest version of SPSS and statistical tests were applied as per the types of variables. All the variables with p-value <0.05 in bivariate analysis were tested for collinearity before taking to multivariate analysis. Variables such as hypertension, diabetes mellitus, dyslipidemia, smoking, sedentary physical activity and obesity had VIF <2, and were thus taken for multivariate analysis using logistic regression. Adjusted Odds Ratio (AOR) was calculated along with its 95% confidence interval in multivariate analysis.

Results

This study included 155 female patients with anginal chest pain in case arm and 155 females who came to medical or cardiology OPD department for general health check up who were otherwise normal individuals, in the control arm. As shown in table 1, the average

age of cases was 60.50 ± 11.13 years and 60.37 ± 10.68 years for controls with p-value of 0.913. Among both cases and controls , there were 39 (25.2%) premenopausal patients each. There were total of 83 (53.3%) hypertensive cases in case arm as compared to 62 (40.0%) in control arm with a p-value of 0.017. There were 54 (34.8%) diabetic patients among cases as compared to 22 (14.2%) in control arm with a significant p value of < 0.001. There were 45 (29.0%) dyslipidemic patients with angina as compared to 20 (12.9%) among controls with a p<0.001. Among cases with angina, the mean LDL level was 97.30 ± 31.89 mg/dl compared to 90.34 ± 20.50 mg/dl in control arm with p=0.023. Similarly, the mean HDL level was 48.55 ± 12.09 mg/dl among cases compared to 52.26 ± 5.07 mg/dl in control arm with p=0.001.

There were 34 (21.9%) smokers among cases compared to 15 (9.7%)among controls with p value of 0.003. Four (2.6%) patients had family history of premature CAD among cases . There were 15 (9.7%) patients with sedentary habit as compared to seven (4.5%) among controls (p=0.077). There were 69 (44.5%) cases with obesity/overweight (BMI >/=23 kg/m2) in case arm as compared to 37 (23.9%) in control arm with a p value of less than 0.001.

Table 1. Comparison of baseline and risk characteristics among cases and controls

Variables	Cases (n=155) (%)	Controls (n=155) (%)	Total (n=310) (%)	Unadjusted OR (95% CI)	p-value
Age group					
≤60 years	77 (49.7)	84 (54.2)	161 (51.9)	0.834 (0.534 - 1.303)	0.426
>60 years	78 (50.3)	71 (45.8)	149 (48.1)	Ref.	
Menstrual status					
Pre-menstrual	39 (25.2)	39 (25.2)	78 (25.2)	1.000 (0.599 - 1.670)	1.000
Post-menstrual	116 (74.8)	116 (74.8)	232 (74.8)	Ref.	
Smoking status					
Smoker	34 (21.9)	15 (9.7)	49 (15.8)	2.623 (1.363 - 5.046)	0.003
Non-smoker	121 (78.1)	140 (90.3)	261 (84.2)	Ref.	
Physical activity					
Sedentary	15 (9.7)	7 (4.5)	22 (7.1)	2.265 (0.897 - 5.721)	0.077
Non-sedentary	140 (90.3)	148 (95.5)	288 (92.9)	Ref.	
Hypertension					
Present	83 (53.3)	62 (40.0)	145 (46.8)	1.729 (1.102 - 2.713)	0.017
Absent	72 (46.5)	93 (60.0)	165 (53.2)	Ref.	
Diabetes					
Present	54 (34.8)	22 (14.2)	76 (24.5)	3.232 (1.848 - 5.654)	<0.001
Absent	101 (65.2)	133 (85.8)	234 (75.5)	Ref.	
Family history of premature CAD					
Present	4 (2.6)	0 (0.0)	4 (1.3)	-	0.061
Absent	151 (97.4)	155 (100.0)	306 (98.7)	-	
BMI (kg/m^2)					
Normal	86 (55.5)	118 (76.1)	204 (65.8)	Ref.	<0.001
Overweight/ Obese(>/=kg/m^2)	69 (44.5)	37 (23.9)	106 (34.2)	2.559 (1.573 - 4.162)	
Dyslipidemia					
Present	45 (29.0)	20 (12.9)	65 (21.0)	2.761 (1.540 - 4.951)	<0.001
Absent	110 (71.0)	135 (87.1)	245 (79.0)	Ref.	
Total	155 (100)	155 (100)	310 (100)		

Table 2. Comparison of mean and standard deviation statistics for cases and controls (total N=310)

Variables	Case(n=155) (Mean ± SD)	Control(n=155) (Mean ± SD)	p - value
Age (in years)	60.50 ± 11.13	60.37 ± 10.68	0.913
BMI (kg/m^2)	23.69 ± 3.42	23.40 ± 3.11	0.434
LDL (mg/dl)	97.30 ± 31.89	90.34 ± 20.50	0.023
HDL (mg/dl)	48.55 ± 12.09	52.26 ± 5.07	0.001
TG (mg/dl)	148.75 ± 84.73	143.05 ± 25.18	0.423
Total cholesterol (mg/dl)	178.80 ± 45.54	184.30 ± 27.94	0.201

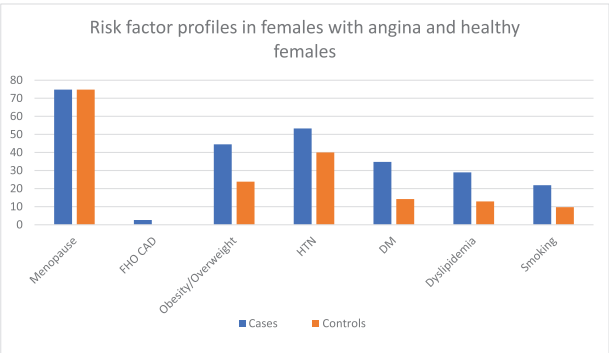

Figure 1-Showing risk factor profiles (%) in cases and controls.

All the variables with p-value <0.05 in bivariate analysis were tested for collinearity before taking to multivariate analysis.Variables such as hypertension, diabetes mellitus, dyslipidemia, smoking and obesity had VIF <2, and were thus taken for multivariate analysis using logistic regression. Adjusted Odds Ratio (AOR) was calculated along with its 95% confidence interval in multivariate analysis.

Table 3. Multivariate analysis of risk factors associated with IHD

Variables	Beta coefficient	Adjusted OR (AOR) (95% CI)	p - value
Smoker	1.160	3.190 (1.606 - 6.334)	0.001
Presence of hypertension	0.256	1.291 (0.788 - 2.115)	0.310
Presence of diabetes	0.945	2.573 (1.346 - 4.918)	0.004
Overweight/ Obesity	0.909	2.482 (1.475 - 4.176)	0.001
Dyslipidemia	0.414	1.513 (0.765 - 2.993)	0.234
Constant	-0.911	0.402	<0.001

In this analysis, females with angina had a slightly higher odds of having HTN with AOR of 1.291 with statistically insignificant p value(p=0.310).

Diabetic females were almost 2.6 times more likely to have angina than those without DM with AOR=1.573,with significant p-value of 0.004.

Interestingly, dyslipidemic females are only at 1.5 times higher odds of having angina with AOR=1.513 and p=0.234.

Additionally, female smokers were almost at 3.2 times higher odds of having angina with AOR=3.190 and p=0.001.

Obese/overweight females were at higher risk of developing angina with AOR=2.482 and a statistically significant p value(p=0.001).

Discussion

Angina pectoris is an important manifestation of IHD which usually, in females, is atypical in type. In our study, we compared the presence of risk factors for IHD in females with anginal chest pain with otherwise healthy females. We compared traditional risk factors like- hypertension, diabetes mellitus, dyslipidemia, smoking, obesity/ overweight, sedentary lifestyle, postmenopausal status and also the family history of premature CAD in these two sets of population.

The multivariate analysis after correcting for confounders showed that the important risk factors for IHD that can be associated significantly with chance of having angina in females are diabetes, smoking and overweight/obesity.Additionally, the analysis also yielded the fact that those with HTN, dyslipidemia were also more likely to have angina than their healthy counterparts, though the finding was statistically insignificant but could be clinically significant if it was done in larger population.

In our multivariate analysis of those important risk factors of IHD with p<0.05 in bivariate analysis above, not all traditional risk factors of IHD were significantly associated with angina in females.The prevalence of HTN in females goes up with age (upto 70-80 %) once they are beyond 60 years of age.[24] HTN is a stronger predictor of CAD in women than in men.[25] In our study females with HTN were 1.291 times more likely to have angina/IHD than those without HTN. However in multivariate analysis, it was not statistically significant (p=0.310) but still there was a trend towards having angina/IHD. In a study done in Malaysian women, HTN was not found to be a significant risk factor of IHD also.[26] However this could have been significant if done in large scale female population. This might also indirectly reflect the higher burden of HTN in normal females or could be a result secondary to white coat HTN or even due to small sample size.

The rise in risk of IHD in patients with diabetes is more in females as compared to males. Women with type 1 DM have more than eight times risk of MI.[27] In one study, women with DM were twice likely to have IHD as compared to normal females.[26] In our study, diabetic females were almost 2.6 times more likely to have angina/IHD than their normal counterparts which was statistically significant(p=0.004).

Dyslipidemia is one important risk factor for IHD. Low LDL is stronger predictor of coronary risk in females than in males. TG raises the coronary risk in females especially elderly ones.[28] Studies done by Frikke-Schmidt and Lee et al. revealed that low level of HDL-cholesterol in plasma raises the risks of IHD and HDL-C is a stronger predictor of IHD in females as compared to LDL-cholesterol level.[29] In our study, dyslipidemic females in total , in multivariate analysis, were 1.5 times more likely to have angina/IHD than their healthy counterparts which was though not statistically significant finding as suggested by p=0.234 but could have been significant if the population size was larger as there was a trend towards having angina/IHD.

Smoking was associated with nearly one-half of all coronary events in females in one study.[30] The risk for myocardial infarction for female smokers is increased more than three times compared with non-smokers.[25] Stopping smoking in women was associated with a rapid decline in the risk of myocardial infarction. In a study of 910 cases with a 1st episode of myocardial infarction, the relative risk was 3.6 among current smokers versus 1.2 in ex-smokers.[31] In our study, smoker females were almost 3.2 times more likely to have angina/IHD compared to their nonsmoker counterparts with a statistically significant p-value of 0.001. This supports smoking as an important risk factor of angina.

Moderate intensity exercise has a beneficial effect against IHD and all-cause mortality. Higher fitness and activity levels in females are predictive of freedom from all causes of mortality, CHD, and stroke. Physical inactivity is more common among women than men. In one study of females, the population risk of heart disease attributable to physical inactivity outweighed that of other traditional IHD risk factors.[32] In our study, we did not find any significant association between sedentary habit and occurrence of angina after bivariate analysis (p=0.077). This could be because of small sample size.

Obesity is linked with many risk factors for atherosclerosis and cardiovascular mortality. The significance of obesity as a coronary risk factor was seen in the prospective cohort Nurses Health Study of about 115,000 females.[33] The heightened risk is also seen with increasing weight within the normal range but is more with obesity. Weight gain after the age of eighteen is also a graded risk factor.[34] Females mainly accumulate subcutaneous fat, whereas males accumulate more visceral fat. Many CVD risk factors are associated with overweight and obesity. Especially, hypertension has a strong association with being overweight (OR=2.1) and obese (OR=5.2) in females, and diabetes has a strong association with abdominal obesity (OR=3.9) in females.[32] In our study, obesity/overweight(BMI>/=23 KG/m2) females were 2.48 times more likely to have angina as compared to those without obesity/overweight with p=0.001, a finding concordant with above mentioned studies.

In an observational study done in Nepalese female patients with angina, the most prevalent risk factor was HTN (43.87%)[35], however ,in our study,the statistically significant risk factors for IHD that were found in females with angina were-Smoking (AOR=3.190,95% CI:1.606, 6.334 and p=0.001),Diabetes (AOR=2.573,95% CI: 1.346, 4.918 and p=0.004),and Obesity/overweight (AOR=2.482,95% CI: 1.475, 4.176 and p=0.001).

Conclusion

The important risk factors for IHD that are associated significantly with likelihood of having angina in Nepalese females are smoking, diabetes mellitus and overweight/obesity in our study. This may assist in optimizing medications and deciding on whether to go for coronary intervention in Nepalese females with angina.

Limitations

The sample size and the duration of the study, if were larger and longer, more statistically significant risk factors for IHD could have been discovered. we have only included traditional risk factors for IHD, not the novel ones such as-hsCRP, Lp(a), homosysteine level etc.

Conflict of interest:

none

References

1. Ford ES, Capewell S. Coronary heart disease mortality among young adults in the U.S. From 1980 through 2002: Concealed leveling of mortality rates. J Am Coll Cardiol 2007;50:2128 32. https://doi.org/10.1016/j.jacc.2007.05.056 PMid:18036449
2. Ford ES, Capewell S. Coronary heart disease mortality among young adults in the United States from 1980 through 2002: Unfavourable developments in recent years. Circulation 2007;115:E292 -
3. Flegal KM, Carroll MD, Ogden CL, Curtin LR. Prevalence and trends in obesity among US adults, 1999-2008. Jama. 2010;303(3):235-41. https://doi.org/10.1001/jama.2009.2014 PMid:20071471 PMCid:PMC3489126
4. Huxley R, Barzi F, Woodward M. Excess risk of fatal coronary heart disease associated with diabetes in men and women: meta-analysis of 37 prospective cohort studies. Bmj. 2006;332(7533):73-8. https://doi.org/10.1136/bmj.38678.389583.7C PMid:16371403 PMCid:PMC1326926
5. Gami AS, Witt BJ, Howard DE, Erwin PJ, Gami LA, Somers VK, et al. Metabolic syndrome and risk of incident cardiovascular events and death: a systematic review and meta-analysis of longitudinal studies. J Am Coll Cardiol. 2007;49(4):403-14. https://doi.org/10.1016/j.jacc.2006.09.032 PMid:17258085
6. Nonnemaker J, Rostron B, Hall P, MacMonegle A, Apelberg B. Mortality and economic costs from regular cigar use in the United States, 2010. Am J Public Health. 2014;104(9):e86-91. https://doi.org/10.2105/AJPH.2014.301991 PMid:25033140 PMCid:PMC4151956
7. Stone NJ, Robinson JG, Lichtenstein AH, Goff DC, Lloyd-Jones DM, Smith SC, et al. Treatment of blood cholesterol to reduce atherosclerotic cardiovascular disease risk in adults: synopsis of the 2013 American College of Cardiology/American Heart Association cholesterol guideline. Ann Intern Med. 2014;160(5):339-43. https://doi.org/10.7326/M14-0126 PMid:24474185
8. Reuterwall C, Hallqvist J, Ahlbom A, De Faire U, Diderichsen F, Hogstedt C, et al. Higher relative, but lower absolute risks of myocardial infarction in women than in men: analysis of some major risk factors in the S heep study. J Intern Med. 1999;246(2):161-74. https://doi.org/10.1046/j.1365-2796.1999.00554.x PMid:10447785
9. Lerner DJ, Kannel WB. Patterns of coronary heart disease morbidity and mortality in the sexes: a 26-year follow-up of the Framingham population. Am Heart J. 1986;111(2):383-90. https://doi.org/10.1016/0002-8703(86)90155-9
10. Hokanson JE, Austin MA. Plasma triglyceride level is a risk factor for cardiovascular disease independent of high-density lipoprotein cholesterol level: a metaanalysis of population-based prospective studies. J Cardiovasc Risk. 1996;3(2):213-9. https://doi.org/10.1097/00043798-199604000-00014 PMid:8836866
11. Wenger NK, Speroff L, Packard B. Cardiovascular health and disease in women. N Engl J Med. 1993;329(4):247-56. https://doi.org/10.1056/NEJM199307223290406 PMid:8316269
12. Hine C, Fenton S, Hughes AO, Velleman G. Coronary heart disease and physical activity in South Asian women: local context and challenges. Health Educ J. 1995;54(4):431-43. https://doi.org/10.1177/001789699505400406

13. McKeigue PM, Marmot MG, Cottier DE, Rahman S, Riemersma RA. Diabetes, hyperinsulinaemia, and coronary risk factors in Bangladeshis in east London. Heart. 1988;60(5):390-6. https://doi.org/10.1136/hrt.60.5.390 PMid:3060188 PMCid:PMC1216596

14. Raut R, KC MB, Sharma D, Rajbhandari S, Baidhya SG, Dhungana M, et al. Comparative Study of Risk Factors Among the Male and Female Patients with Acute Myocardial Infarction Admitted in CCU of Sahid Gangalal National Heart Centre. Nepal Heart J. 2009;6(1):4-7. https://doi.org/10.3126/njh.v6i1.18446

15. Schnohr P, Jensen JS, Scharling H, Nordestgaard BG. Coronary heart disease risk factors ranked by importance for the individual and community. A 21 year follow-up of 12000 men and women from The Copenhagen City Heart Study. Eur Heart J. 2002;23(8):620-6. https://doi.org/10.1053/euhj.2001.2842 PMid:11969276

16. Bogati A, Manandhar R, Sharma D, Baidhya SG, Prajapati D, Baniya S, et al. Prevalence of cardiovascular risk factors among the residents of urban community of Kathmandu municipality. Nepal Heart J. 2017;14(1):3-7. https://doi.org/10.3126/njh.v14i1.17187

17. Diamond GA. A clinically relevant classification of chest discomfort. Journal of the American College of Cardiology. 1983 Feb;1(2 Part 1):574-5. https://doi.org/10.1016/S0735-1097(83)80093-X

18. Third Report of the National Cholesterol Education Program (NCEP). Expert panel on detection, evaluation, and treatment of high blood cholesterol in adults (adult treatment panel III) final report. Circulation. 2002;106(25):3143-421. https://doi.org/10.1161/circ.106.25.3143 PMid:12485966

19. Sivapalaratnam S, Boekholdt SM, Trip MD, Sandhu MS, Luben R, Kastelein JJ, Wareham NJ, Khaw KT. Family history of premature coronary heart disease and risk prediction in the EPIC-Norfolk prospective population study. Heart. 2010 Dec 15;96(24):1985-9. https://doi.org/10.1136/hrt.2010.210740 PMid:20962344 PMCid:PMC3773915

20. American Diabetes Association. 2. Classification and diagnosis of diabetes: Standards of Medical Care in Diabetes-2020. Diabetes care. 2020 Jan 1;43(Supplement_1):S14-31. https://doi.org/10.2337/dc20-S002 PMid:31862745

21. James PA, Oparil S, Carter BL, Cushman WC, Dennison-Himmelfarb C, Handler J, Lackland DT, LeFevre ML, MacKenzie TD, Ogedegbe O, Smith SC. 2014 evidence-based guideline for the management of high blood pressure in adults: report from the panel members appointed to the Eighth Joint National Committee (JNC 8). Jama. 2014 Feb 5;311(5):507-20. https://doi.org/10.1001/jama.2013.284427 PMid:24352797

22. Misra A, Chowbey P, Makkar BM, Vikram NK, Wasir JS, Chadha D, et al. Consensus statement for diagnosis of obesity, abdominal obesity and the metabolic syndrome for Asian Indians and recommendations for physical activity, medical and surgical management. Japi. 2009;57(2):163-70.

23. Eckel RH, Jakicic JM, Ard JD, de Jesus JM, Houston Miller N, Hubbard VS, Lee IM, Lichtenstein AH, Loria CM, Millen BE, Nonas CA. 2013 AHA/ACC guideline on lifestyle management to reduce cardiovascular risk: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. Journal of the American college of cardiology. 2014 Jul 1;63(25 Part B):2960-84. https://doi.org/10.1016/j.jacc.2013.11.003

24. Egan BM, Zhao Y, Axon RN. US trends in prevalence, awareness, treatment, and control of hypertension, 1988-2008. Jama. 2010;303(20):2043-50. https://doi.org/10.1001/jama.2010.650 PMid:20501926

25. Millett ER, Peters SA, Woodward M. Sex differences in risk factors for myocardial infarction: cohort study of UK Biobank participants. bmj. 2018;363. https://doi.org/10.1136/bmj.k4247 PMid:30404896 PMCid:PMC6364292

26. Rashid NA, Nawi AM, Khadijah S. Exploratory analysis of traditional risk factors of ischemic heart disease (IHD) among predominantly Malay Malaysian women. BMC Public Health. 2019;19(4):1-8. https://doi.org/10.1186/s12889-019-6855-5 PMid:31196022 PMCid:PMC6565533

27. Jousilahti P, Vartiainen E, Tuomilehto J, Puska P. Sex, age, cardiovascular risk factors, and coronary heart disease: a prospective follow-up study of 14 786 middle-aged men and women in Finland. Circulation. 1999;99(9):1165-72. https://doi.org/10.1161/01.CIR.99.9.1165 PMid:10069784

28. Rich-Edwards JW, Manson JE, Hennekens CH, Buring JE. The primary prevention of coronary heart disease in women. N Engl J Med. 1995;332(26):1758-66. https://doi.org/10.1056/NEJM199506293322607 PMid:7760894

29. Frikke-Schmidt R. Genetic variation in the ABCA1 gene, HDL cholesterol, and risk of ischemic heart disease in the general population. Atherosclerosis. 2010;208(2):305-16. https://doi.org/10.1016/j.atherosclerosis.2009.06.005 PMid:19596329

30. Willett WC, Green A, Stampfer MJ, Speizer FE, Colditz GA, Rosner B, et al. Relative and absolute excess risks of coronary heart disease among women who smoke cigarettes. N Engl J Med. 1987;317(21):1303-9. https://doi.org/10.1056/NEJM198711193172102 PMid:3683458

31. Rosenberg L, Palmer JR, Shapiro S. Decline in the risk of myocardial infarction among women who stop smoking. N Engl J Med. 1990;322(4):213-7. https://doi.org/10.1056/NEJM199001253220401 PMid:2294448

32. Mehta PK, Wei J, Wenger NK. Ischemic heart disease in women: a focus on risk factors. Trends Cardiovasc Med. 2015;25(2):140-51. https://doi.org/10.1016/j.tcm.2014.10.005 PMid:25453985 PMCid:PMC4336825

33. Willett WC, Manson JE, Stampfer MJ, Colditz GA, Rosner B, Speizer FE, et al. Weight, weight change, and coronary heart disease in women: risk within the'normal'weight range. Jama. 1995;273(6):461-5.
https://doi.org/10.1001/jama.1995.03520300035033
PMid:7654270

34. Manson JE, Willett WC, Stampfer MJ, Colditz GA, Hunter DJ, Hankinson SE, et al. Body weight and mortality among women. N Engl J Med. 1995;333(11):677-85.
https://doi.org/10.1056/NEJM199509143331101
PMid:7637744

35. Adhikari S, Gajurel RM, Poudel CM, Shrestha H, Thapa S, Devkota S, Manandhar B, Khanal R, Shakya S, Yadav V, Sharma M. Study of clinical profiles, risk factors and coronary angiographic patterns in female patients presenting with anginal chest pain in a tertiary care centre of Nepal. Nepalese Heart Journal. 2022 Nov 21;19(2):13-8.
https://doi.org/10.3126/njh.v20i2.48868