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

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Abstract

Background and Aims: Coronary artery disease is one of the important causes of deaths in females in many countries. Females with chest pain are more likely to be treated in a different way as compared to males at the time of presentation. Worldwide, there has been a considerable rise in the number of females who are undergoing coronary angiography recently.

Methods: This study was a single-centre, prospective, observational study conducted in the department of cardiology, MCVTC, Tribhuvan University, Nepal. The study period was from 5th July 2020 to 4th July 2021.155 female patients with anginal chest pain were enrolled. Data were collected after thorough history taking, physical examination, laboratory investigations, and coronary angiography. They were further divided into three age groups:<50 years,50-65 years and >65 years. Subsequently statistical analysis was done using latest version of SPSS.

Results: The mean age of the patients was 59.64 years (SD=11.428). There were 119 (76.77%) postmenopausal patients. The most prevalent risk factor of IHD was HTN (43.87%). Obesity/overweight was most common (58.62%) in those with age <50 years. DM was most common (26.32%) in age group 50-65 years. HTN was the most prevalent (52.63%) in age group 50-65 years. The maximum proportion of dyslipidemic patients (34.21%) were found in age group 50-65 years. 52.25% patients presented with acute coronary syndrome. 33.55% patients had normal coronary arteries. 11.61% patients had nonobstructive coronary artery disease.

Obstructive coronary artery disease was found in 51.61% patients. In patients with obstructive CAD, LAD was the most commonly involved vessel followed by RCA .

Conclusion: Findings from our study shows higher prevalence of risk factors for IHD in Nepalese females. This study also demonstrates that as females get older and become postmenopausal, the number of risk factors for CAD increases. Understanding the risk factors for CAD and angiographic patterns in females could be helpful in implementing optimal treatment strategies in females with angina.

Keywords: Angina, Females, Ischemic heart disease, Risk factors.

Introduction

Coronary artery disease (CAD) is one of the important causes of deaths in females. Unlike the previously thought concept that coronary artery disease mainly affects males more than females, recent studies are showing that for last few years overall prevalence of CAD in females is rising.[1-4] The increase in coronary deaths among young adults is because of the rise in unfavorable coronary risk factors in current scenario and this is particularly notable among females.[5,6] Two of every three women have at least one of the classic/tradi-

tional risk factors for heart disease: age >55 years, family history of premature heart disease, tobacco smoking, hypertension(HTN), dyslipidemia, obesity, and diabetes mellitus. Some risk factors have been shown to be more causally related to CAD in women. These include diabetes, metabolic syndrome, low high density lipoprotein cholesterol and smoking.[7-10] Unlike the linear rise in CAD in males as they age, there is exponential rise in CAD in females after the age of 60 years.[11] Globally, there has been a considerable increase in the number of females undergoing coronary angiography over previous

years. Multiple reasons could be responsible for this rise. To identify these changes adequately clinico-angiographic profiles of females undergoing coronary angiography should be understood. There are very few studies which describe the pattern and prevalence of CAD in women planned for coronary angiography (CAG). Occlusion of left main coronary artery (LMCA) is not so common but an important cause of death and morbidity. The burden due to left main disease (LMD) has not been well searched for in females. Also the plan for stent placement in the interventions involving LMCA depends mainly on patterns of CAD. So study of angiographic patterns of CAD in females may help guide for exploring new strategies in terms of coronary intervention percutaneously.[12]

Methods

This was a single centre, prospective, observational study. The study period was from 5th July 2020 to 4th July 2021. All consecutive female patients undergoing coronary angiography in the department of Cardiology of MCVTC, IOM with anginal chest pain secondary to suspected CAD over a period of one year were considered for participation in the study. All female patients presenting with anginal chest pain and age >16 years and < 85 years were included in the study. Patients not willing to give consent, those with chronic kidney disease, valvular heart disease, cardiomyopathy, pulmonary arterial hypertension, congenital heart disease, pregnancy, those with noncardiac causes of chest pain (infective and traumatic), those with unstable medical and psychiatric illnesses were excluded. Patients were divided into three age groups: :<50 years,50-65 years and >65 years. Study variables were: Age, Sex, body mass index(BMI), smoking, menopause, physical activity, Lipid profile, Blood glucose profile, Troponin-I, ECG, left ventricular ejection fraction(LVEF),treadmill test(TMT),Name and number of coronary artery/arteries involved, patterns of coronary angiographic lesions. A proforma questionnaire method was applied to obtain required data.

More relevant data were obtained from the coronary angiographic findings and the results of tests done. Data collection from patients included in the study were done using questionnaires, physical assessment, laboratory parameters, coronary angiography.

The type of angina was classified as typical or atypical angina.[13] Typical angina was labeled 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 symptoms were classified as atypical angina. If one or none of the criteria was present, the pain was classified as noncardiac chest pain. 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.[14] Positive family history of CAD was considered if first degree relatives had CAD before the age of 65 years in women.[15] Diabetes Mellitus(DM) 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 as per ADA guidelines-2020.[16] Hypertension was defined as systolic blood pressure >140 and/or diastolic >90 mmHg and/or on anti-hypertensive treatment as per JNC-8 guidelines. Obesity was defined as per Asian-Indian consensus guidelines-2009.[17] Physical activity or exercise for <150 min/week was used as the criteria for defining sedentary life style[18].STEMI was defined as new ST elevation at the J point in two contiguous leads of >0.1 mV in all leads other than leads V2-V3. For leads V2-V3 the following cut points apply: ≥0.2 mV in

men ≥40 years, ≥0.25 mV in men <40 years, ≥0.15 mV in women. Acute coronary syndrome (ACS) patients were then categorized into ST-segment elevation myocardial infarction (STEMI) or NSTEMI/UA. Patients were subjected for Echocardiography (GE, Vivid 7) to look for Left ventricular systolic dysfunction. The Echocardiography parameters for LV Systolic function was measured as per guideline from American Society of Echocardiography, for females- normal: (54-74%), mild dysfunction: (41-53%),moderate dysfunction: (30-40%), severe dysfunction: <30%. Coronary angiogram(CAG) was used to establish the cause and guide therapy. CAG was performed using Philips and siemens C-arms through radial or femoral arterial approach. At least two orthogonal views were obtained for each vessel. Significant CAD was defined as a diameter stenosis >50% in each major epicardial artery. CAD was expressed as Minor CAD (if <50% luminal Stenosis). Patients were classified as having single-vessel disease (SVD), double-vessel disease (DVD) or triple vessel disease (TVD) and left main disease(LMD) accordingly.

Data were recorded and entered in an excel sheet and analyzed using SPSS latest version and statistical tests were used according to the types of variables.

Results

This study included 155 female patients with anginal chest pain. As shown in table 1,The average age of patients was 59.64 ± 11.428 years.

Table1: Baseline, clinical and risk factor profiles of the patients

Characteristics	Total (n=155) (%)	<50 years	50-65 years	>65 years
Postmenopausal	119 (76.77%)	0 (0%)	69 (90%)	50 (100%)
>/=3 risk factors	53 (34.19%)	6 (20.69%)	26 (34.21%)	21 (42%)
Sedentary lifestyle	16 (10.32%)	0 (0%)	2 (2.63%)	14 (28%)
Obesity/over-weight-BMI>/=23kg/m2	66 (42.58%)	17 (58.62%)	34 (44.74%)	15 (30%)
Diabetes Miletus	40 (25.81%)	7 (24.14%)	20 (26.32%)	13 (26%)
Hypertension	68 (43.87%)	8 (27.59%)	40 (52.63%)	20 (40%)
Dyslipidemia	49 (31.61%)	8 (27.59%)	26 (34.21%)	15 (30%)
Smoking	33 (21.29%)	0 (0%)	17 (22.37%)	16 (32%)
Family history of premature CAD	5 (3.23%)	2 (6.9%)	1 (1.32%)	2 (4%)
Abnormal ECG -Yes	9 (31.03%)	31 (40.79%)	38 (76.00%)	78 (50.32%)
TMT in non ACS patients -positive	37 (23.87%)	14 (48.28%)	22 (28.95%)	1 (2%)
LVdysfunction (LVEF<54%)	45 (29.03%)	6 (20.69%)	15 (19.74%)	24 (48%)

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Table 2: Pattern of presentations of females with anginal chest pain

Presenting diagnosis	Total (n=155) (%)	<50 years	50-65 years	>65 years
AWSTEMI	12 (7.74%)	4 (13.79%)	4 (5.26%)	4 (8%)
IWSTEMI	17(10.97%)	2 (6.9%)	11 (14.47%)	4 (8%)
NSTEMI	37 (23.87%)	1 (3.45%)	11 (14.47%)	25 (50%)
UA	15 (9.68%)	3 (10.34%)	7 (9.21%)	5 (10%)
CSA	35 (22.58%)	4 (13.79%)	21 (27.63%)	10 (20%)
ATCP	39 (25.16%)	15 (51.72%)	22 (28.95%)	2 (4%)

STEMI:ST elevation myocardial infarction, AWSTEMI:Anterior wall STEMI, IWSTEMI:Inferior wall STEMI

NSTEMI:Non ST elevation myocardial infarction, UA:Unstable angina, CSA:Chronic stable angina, ATCP:Atypical chest pain

Out of 155 patients,81(52.25%) patients presented with acute coronary syndrome and 74(47.75%) presented with chronic stable angina and atypical angina.

18.7%) cases with angina presented with STEMI. NSTEMI was the presenting diagnosis in 37 (23.87%) patients in total. UA was the presenting diagnosis in 15 (9.68%) patients in total. CSA was the presenting diagnosis in 35 (22.58%) patients in total. Atypical chest pain(ATCP) was the presenting diagnosis in 39 (25.16%) patients in total.

Abnormal resting ECG pattern was found in about 78(50.32%) cases. Treadmill test was positive in 37 patients which is about 50% of total patients with non-ACS presentation(total number of patients with non-ACS presenation was 74). Among all, 45 (29.03%) patients had evidence of LV dysfunction at presentation.

Table 3: Angiographic patterns in females with angina.

ANGIOGRPAHIC PATTERNS				
Characteristics	Total	<50 years	50-65 years	>65 years
Normal coronaries	52 (33.55%)	18 (62.07%)	29 (38.16%)	5 (10%)
Nonobstructive disease	18 (11.61%)	2 (6.9%)	10 (13.16%)	6 (12%)
Obstructive diseases	80 (51.61%)	7 (24.14%)	35 (46.05%)	38 (76%)

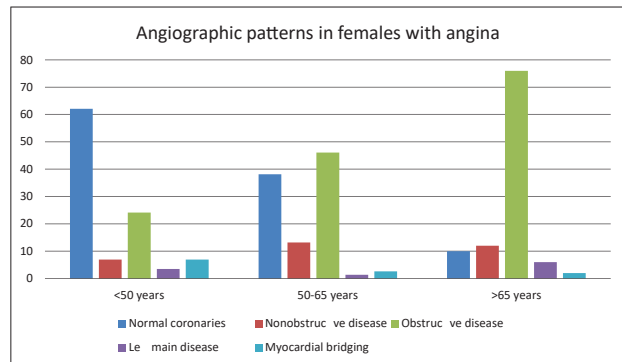|				
SVD	18 (11.61%)	3 (10.34%)	10 (13.16%)	5 (10.00%)
DVD	36 (23.23%)	2 (6.89%)	17 (22.37%)	17 (34.00%)
TVD	26 (16.77%)	2 (6.89%)	8 (10.53%)	16 (32.00%)
Left main disease(LMD) 5 (3.23%)		1 (3.45%)	1 (1.32%)	3 (6%)
Myocardial bridging only 5 (3.23%)		2 (6.9%)	2 (2.63%)	1 (2%)

Figure 1-Angiographic patterns in females with angina.

Table 4. Individual vessel involvement in obstructive CAD

Vessel involved		Number	Percentage
LAD(Left anterior descending artery) stenosis	No	89	57.4
	Yes	66	42.6
	Total	155	100.0
RCA (Right coronary artery) stenosis	No	98	63.2
	Yes	57	36.8
	Total	155	100.0
LCX (Left circumflex artery) stenosis	No	112	72.3
	Yes	43	27.7
	Total	155	100.0

Out of all who underwent CAG, five (3.23%)patients had evidence of left main disease, with most frequent, three (6%) in group C. All those cases were associated with triple vessel disease.

Lastly, five (3.23%) patients had evidence of myocardial bridging with normal coronaries, with most frequent, two (6.9%) in group A.

Discussion

There is an increasing trend of incidence and prevalence of ischemic heart disease in famale population in today's world because of various factors including lifestyle changes. Cardio vascular disease is one of the leading causes of deaths in females. The incidence of myocardial infarction goes up drastically after

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menopause in females.[11] Among various manifestations of ischemic heart disease, angina pectoris is one important manifestation which usually, if occurs in females, is atypical in nature. IHD is not common in premenopausal women if there are no other accompanying risk factors for IHD.[19] ACC/AHA guidelines recognize menopause as a risk factor for IHD, equivalent to male sex.[20,21] The prevalence of HTN in females increases with age and can reach upto 70-80 % once they are older than 60 years of age.[22] It is a stronger predictor of CAD in females than in males.[23] Patients were categorized in three age groups:<50 years,50-65 years and >65 years. The average age of menopause in Nepalese female population is 48.7 years so the lower cutoff of 50 years was selected.[24] The relative difference in CHD risk between the sexes was largest among the youngest subjects (25 to 49 years), but the absolute difference was largest in the older age group due to a higher prevalence (60 to 64 years) hence the upper cut off of 65 years was selected.[25] Most of the studies have taken two groups in the past.One study in India studied among three groups had categorized age group as less than 45,45-55 and more than 55 years.[26] In our study, majority of patients were in the age group 50-60 years and in the postmenopausal groups which is a similar finding as in many studies in the past.[12,27] This indicates most of the patients with older age are more likely to have anginal symptoms and hence likely to under go CAG. Among three groups, the one with age >65 years has maximum proportion of patients with >/=3 risk factors, a similar finding found in one study done in Indian females.[26] Sedentary lifestyle was observed with maximum proportion in those with age >65years which probably reflects associated disabilities related to increasing age and also the changes in the lifestyles.

Obesity/overweight was found with maximum proportion in those with age <50 years. This was unlike in most of the past studies12, but similar to one study from India.26 This could be due to the fact that we used the criteria for Asian population with cut off BMI>/= 23 kg/m2. This also implies an increasing trend of obesity or overweight in females because of inappropriate lifestyle patterns.

HTN and diabetes were found with maximum proportion in the age group 50-65 years. This shows that there was increasing prevalence of these two important risk factors of IHD in females with angina as they grow older. This finding was similar to various studies from the past.[12,27]

Likewise, the maximum dyslipidemic patients were found in age group 50-65 years. In contrast, some studies from the past have shown higher prevalence of dyslipidemia in younger patients[28].

Maximum smoker's proportion was observed in age group >65 years. This was consistent with the findings from a study which also found higher prevalence of smoking in elderly females[26].

Family history of premature CAD was observed more frequently in those with age < 50 years. This was a significant finding and reminds us the importance of family history in young females who present with angina. Females with at least one parent who had myocardial infarction are at four times higher risk of acute coronary syndrome29. Additionally, one study revealed that females whose parents had coronary events during young age (females with <55 years of age) have higher coronary calcium scores[30].

In terms of angina, majority presented with atypical anginal type of chest pain. The atypical angina was more common with young females with age less than 50 years. This was similar finding as in previous studies [31,32].

Majority cases with angina presented with STEMI which was most frequent presentation in females with age group 50-65 years. Likewise NSTEMI was the presenting diagnosis with most females within the age group 50-65years. This reflected the overall higher prevalence of MI in those >50 years of age which was similar to

studies from past[26]. However UA was the most common presenting diagnosis in younger females with age <50 years in our study. CSA was the most common presenting diagnosis in females with age 50-65 years. In terms of ACS, previous studies have not revealed significant differences in the pattern of presentation[12].

In regards to angiographic pattern, interestingly about one-third patients had normal coronary arteries. Most frequently,young females in age group<50 years had normal coronaries. This could be due to higher prevalence of microvascular angina in young females[33]. Apart from this, it could be as a result of atypical presentations in these females and lower threshold of overdiagnosing these as anginal pain leading to consequent interventions. Our prevalence of normal coronaries in young females is similar to one of the studies[34].

In our study, obstructive coronary artery disease was found in about half of the patients with most of them in the age group >65 years. This was similar to findings from WISE study where 43% patients had significant CAD. In another study done by abed et al,55.2% females had obstructive CAD27. Another publication from India revealed that 45.45% of females with age>55 years had evidence of obstructive CAD[12].

In our study, among those with obstructive disease, DVD was the most common angiographic pattern found in CAG. In age group <50 years, SVD was most commonly found, in age group 50-65 years and >65 years, the most common angiographic pattern was DVD. TVD was most commonly encountered in age group >65years. Vesselwise in those with obstructive CAD,LAD was the most commonly involved vessel followed by RCA and LCX respectively. In two studies, similar patterns of vessel involvement were noted where SVD was common in younger females and DVD and TVD in elderly females[12,35].

All cases with left main disease(LMD) were associated with TVD. There are very few studies on prevalence of LMD in females. Our finding is similar to that from a study by ezhumalai et al and kunal et al[12,26]. The prevalence of LMD were 3.4% and 5.2% respectively in those studies and LMD was common among those with age > 55years.

Lastly,the evidence of myocardial bridging with normal coronaries, was most frequent in age group < 50 years , a finding similar to one from Kunal et al in Indian female population[26].

Limitation

The main limitation of this study is small sample size and short time period. The clinical diagnosis of angina can have interpersonal variation, hence the threshold for offering CAG among different physicians can vary. We have only studied traditional risk factors of IHD, not the novel ones due to cost factors and unavailability.

Conclusion

Findings from our study shows higher prevalence of risk factors for CAD in Nepalese females. HTN, dyslipidemia, DM and smoking are more prevalent risk factors of CAD in our study. This study also demonstrates that as females get older and become postmenopausal, the number of risk factors for CAD increases. We also observed the age related differences in the risk factors, clinical factors including angiographic patterns in Nepalese females with angina. Realizing and understanding the risk factors for CAD and angiographic patterns in females will be of paramount importance in implementing optimal treatment strategies.

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Acknowledgment

Conflict of interest
None

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