Prospective analysis of risk factors and angiographic profile in women with coronary artery disease –A hospital based study

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ABSTRACT

Background: In order to facilitate diagnosis and timely intervention, it is essential to understand the presentation pattern of cardiac symptoms, and distribution of risk factors in women with Coronary Artery Disease (CAD). However, limited data is available regarding the salient features of CAD in women like distribution of risk factors and anatomical extent. **Aims and Objective:** The purpose of the present study was to determine the clinical and risk factor profile of women admitted with CAD and to analyze their angiographic findings in relation to the clinical presentation and risk factors in a tertiary care referral center of eastern India. **Materials and Methods:** In this study we prospectively analysed risk factors and angiographic patterns of 140 consecutive female patients who underwent coronary angiography for suspected CAD over a period of 2 years. **Results:** CAD most commonly affected females of age group >60yrs with higher incidence among postmenopausal as compared to premenopausal women. Unstable angina was the commonest presentation among patients with normal coronaries as well as obstructive CAD.A substantial percentage of women presenting with anginal pain were angiographically normal. Hypertension was the most common associated risk factor followed by diabetes, elevated total cholesterol, high LDL & low HDL. Most common coronary angiography finding was single vessel disease. On analysis, diabetes mellitus, elevated cholesterol, elevated LDL & triglycerides were most commonly associated with triple vessel disease. **Conclusion:** The incidence of CAD in females increased with age. Single vessel disease was the commonest presentation with Left Anterior Descending Artery, the most frequently involved vessel.

Key words: Angina; Coronary angiography; Coronary Artery Disease (CAD); Women

INTRODUCTION

In the present century, Coronary artery disease (CAD) is one of the leading cause of mortality among women in both developed and developing countries.[1] In contrast to conventional belief that the disease primarily affecting men, the current data shows an increasing trend of mortality in women due to CAD than men.[2] Also death due to CAD in women outnumbers that of cancers, infections, and accidents combined.[3,4] The worldwide INTERHEART Study, a large cohort study of more than 52000 individuals with myocardial infarction, has revealed that women have their first presentation of coronary heart disease approximately 10 years later than men, most commonly after menopause[5] but the mortality increases as age increases as compared to men of corresponding age group.[6] This increase in mortality among elderly women correlated with the steady increase in unfavourable coronary risk factors, mainly diabetes, hypertension (HTN), and metabolic syndrome.[7,8] Every two of three women have at least one of the classic risk factors for heart disease i.e. age >55 years, family history of premature heart disease, tobacco smoking, HTN, dyslipidaemia, obesity, and diabetes mellitus.[9] Previous studies suggested risk factors

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like diabetes,[10] low highdensity lipoproteincholesterol (HDLC)[11] and smoking,[12] elevated triglycerides[13] were associated with CAD in women. In the Framingham study, low HDLC was shown to be a predictor of CAD, more so in women than men.[11] The presence and severity of CAD in women increases linearly with age which might be due to increased prevalence of established risk factors, hormonal changes and lipid abnormalities associated with menopause and depleted estrogen levels in elderly women, but the exact association remain yet to be proven.[14,15] However, limited data is available regarding study of association of risk factors and angiographic patterns of CAD in Indian women. With this background, in this present study, we aim to analyse the risk factors and angiographic profile of CAD in women presenting with ischemic chest pain in a tertiary care centre like S.C.B. Medical College, Cuttack.

MATERIALS AND METHODS

Aims and Objectives
The Primary objective was to study the distribution of risk factors in women with CAD.

The secondary objective was to analyze the relation between angiographic findings and risk factors in the same patient population.

Study Design
The present study was a prospective and observational study to evaluate clinical and risk factor profiles of women admitted with CAD in department of Cardiology, S.C.B. Medical College, Cuttack, for a period of 2 years. All females who were referred to the hospital for coronary angiography fulfilling inclusion & exclusion criteria were included in the study.

Inclusion criteria
All the female patients presenting with Acute ST elevation Myocardial infarction (STEMI), unstable angina/NSTEMI, chronic stable angina in the IPD &OPD were included in the study.

Exclusion Criteria
Female patients with serious comorbid conditions whom the risk of coronary arteriography outweighs the benefit of the procedure, patients presenting with non-cardiac chest pain (<1 of typical angina characteristics) and patients not willing for revascularization were excluded from the study.

From the female patients, demographic data and detail clinical history were collected by in-person interviews or by reviewing their medical records. The data collection form included age, sex, weight, height, body mass index, laboratory results such as total cholesterol, triglyceride,

FBS, LDL, and HDL, positive history of chronic disease (diabetes, hypertension, and hyperlipidaemia), smoking, family history of ischemic heart disease (first-degree relative), past history of CCU admission, previous history of coronary angiography, prior myocardial infarction, and coronary artery bypass graft or percutaneous transluminal angioplasty. All the patients were subjected to echocardiographic examination before coronary angiography, and the details regarding the presence of regional wall abnormalities, left ventricular dysfunction (Ejection fraction<50%) valvular heart function and pulmonary artery hypertension were noted.

DEFINITIONS

STEMI is defined as patient having any one of following criteria like characteristic chest pain suggestive of ischemia for prolonged period (>30 min) or evolutionary changes in ECG showing ST elevation of at least 1mm in two contiguous limb leads or 2mm in two contiguous chest leads/precordial leads or Characteristic rise or fall of enzymes (CK-MB and troponin) suggestive of myonecrosis Unstable angina/NSTEMI is defined as angina with at least one of the following i.e. occurring at rest(or minimal exertion)usually lasting more than 20 min. or being severe and described as frank pain &of new onset(within 1 month) or ` Occurring with a crescendo pattern. Patients with elevated biomarkers of cardiac necrosis (CPK MB, Troponin) are diagnosed having NSTEMI.The type of angina is classified as typical or atypical. Typical angina is defined according to following criteria (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 nitro-glycerine within minutes. If 1–2 of the criteria were present, the symptoms were classified as atypical angina. If none or of the criteria was present, the pain was classified as noncardiac chest pain. Hypertension was defined as patient on treatment for elevated blood pressure or a systolic pressure ≥140 mm Hg and/or diastolic pressure ≥90 mmHg. Diabetes was defined as fasting blood glucose equal to or >126 mg/dl or 2-h postprandial blood glucose >200 mg/dl or HbA1c ≥6.5% and/or patients with a history of diabetes mellitus or who are receiving antidiabetic therapy. Smoker was defined as the one who regularly smoked an average of one or more cigarettes a day for at least 1 year. Patients who had given up smoking for >12 months were considered ex-smokers. The family history of premature CAD was considered positive in the presence of CAD in a first-degree male relative 55 years or less in age and/or a first degree female relative 65 years or less in age. Patients on lipid-lowering therapy

or lipid levels in the following range were considered to have dyslipidaemia, i.e. total cholesterol >240 mg/dl, triglycerides >150 mg/dl, LDL-cholesterol ≥130 mg/dl and HDL-cholesterol ≤40 mg/dl. Overweight/obesity was labelled in those with a body mass index (BMI) ≥23 kg/m². Physical activity or exercise for <150 min/week was used as the criteria for defining sedentary lifestyle.

The diagnosis of Acute Coronary Syndrome (ACS) was made if the patient presented with new onset symptoms suggestive of ACS within preceding 1 week with any one of the following: i.e. Electrocardiogram (ECG) changes suggestive of myocardial ischemia/infarction, elevated biomarkers of myocardial necrosis (any one of creatine kinase-muscle/brain/ Troponin-T or Troponin-I) or history of documented CAD in the past. ACS patients were categorized into ST-segment elevation myocardial infarction (STEMI) or NSTEMI/UA. STEMI was diagnosed if ECG showed evidence of ST-segment elevation in ≥2 contiguous leads. The rest of the cases were labelled as NSTEMI/UA based on the presence of elevated biomarkers of myocardial necrosis

Coronary angiography

Coronary angiography was performed in our department with Siemens Image Intensifier Based Cath Lab Equipment through the femoral or radial artery approach. A minimum of two orthogonal views were obtained for each vessel. Angiograms were analysed from cine recording and reports were compared with QCA measurements for extent of stenosis. Presence, location and extent of coronary artery disease were noted. The angiographic pattern of coronary arteries was classified according to the number of major coronary arteries involved. It was called single, double, triple vessel disease (TVD) when one, two or three major coronary arteries were with >50% luminal stenosis, respectively. The arterial segments were seen in such views that have minimal overlapping or foreshortening of the lesions. The lesions were graded as Obstructive if ≥50% of the luminal diameter reduction and Nonobstructive disease ≤50% of the luminal diameter reduction and/or irregularities of the lumen or Normal epicardial coronaries if no stenosis and no lumen irregularities.

The study protocol was approved by Institutional Ethical Committee, S.C.B. Medical College, Cuttack. The study was conducted with the patients' understanding and consent. All work was conducted in accordance with the Declaration of Helsinki (1964).

STATISTICAL ANALYSIS

Values are expressed as mean±SD. The data obtained were analysed by SPSS-windows10 software system. Continuous variables were analyzed for statistical significance using the paired t test and discrete variables using the Chi-Square test.

RESULTS

A total 140 no of female patients admitted to our hospital were included in our study. It was found that the mean age of the female patient suffering from CAD was 54.19±9.89yrs and maximum were from >60yrs age group with post-menopausal preponderance (Figure 1).

Sixty eight percentage female showed angiographic evidences of CAD where as 32% patients had normal coronaries on angiography (Figure 2).

Unstable angina was the commonest presentation in both group of patients having normal coronaries and CAD (Figure 3).

Left anterior descending artery (41%) was the commonest vessel involved followed by RCA (29%) and LCX (26%) (Figure 4).

Left Anterior Descending (LAD) is the commonest vessel, 78(41%) involved followed by Right Coronary Artery (RCA) 56 (29%) and Left Circumflex (LCX) 50(26%).
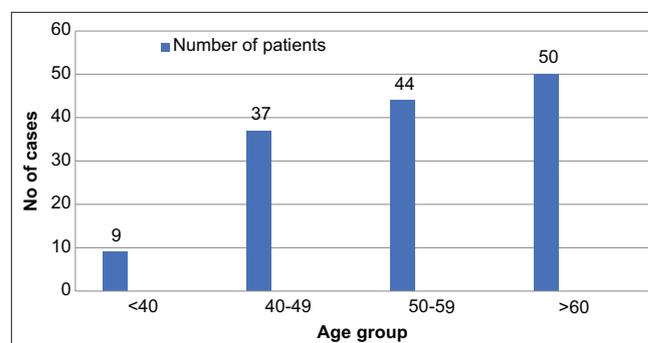

Figure 1: Age wise distribution of coronary artery disease in women
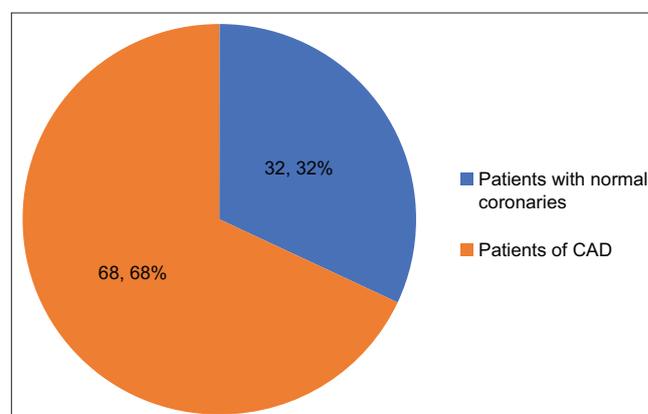

Figure 2: Patients with normal coronaries Vs patients with angiographic evidences of CAD

Out of 49 patients who presented with chronic stable angina had normal coronaries (36%) followed by minor lesion or SVD(22% each).In patients with unstable angina 38% had normal coronaries and SVD as the most common lesion in CAD Most patients who presented with STEMI had SVD (Figure 5).

Coronary artery disease was more common in patients with diabetes (p=0.009), body mass index ≥25kg/m² (p=0.007), family history of premature CAD (p=0.006), total cholesterol ≥200mg/dl (p=0.011), LDL ≥100mg/dl (p=0.006) and HDL ≤40mg/dl (p=0.009). These relations were statistically significant. The others are not statistically significant (Table 1).

Triple vessel disease patients presented more with unstable angina/NSTEMI (p=0.011) which is statistically significant (Table 2).

Triple vessel disease was more commonly associated with diabetes (p=0.0231), total cholesterol ≥200mg/dl (p=0.007). LDL ≥100mg/dl (p=0.002) and TG ≥150mg/

dl (p=0.047). This relation was statistically significant (Table 3).

DISCUSSION

The present study was carried out to assess the clinical and risk factor profile of women admitted with coronary artery disease and analyse the angiographic findings in relation to these risk factors. The mean age in our study was 54.19±9.89years but the maximum no of patients were from>60 years age group. This result coincided with study done by Lekha Adik Pathak 2017[16] where CAD was most prevalent between the age group 60–80 years and out of 3250 patients studied, 65% were post-menopausal and 24% were post hysterectomy. In our study, incidence among postmenopausal (119 patients, (85%) was more as compared to premenopausal (21 patients). Out of 21 premenopausal, 13 (62%) had evidences of coronary artery disease on angiography. In our study, in patients with angiographically evident CAD, risk factor analysis revealed hypertension to be the commonest (52.9%) followed by diabetes (44.3%), tobacco chewing and passive smoking (17%) while in a previous study raised LDL (76%) hypertension (71%), diabetes mellitus (63%), reduced HDL (55%) and obesity (54%) among the associated risk factors. Active smoking was present only in 7% patients. The family history of Coronary artery disease (in 1st degree relatives) was found to be present in 49% of women.[16] Where as in patients with normal coronaries, hypertension was the commonest risk factor 16 (36%) followed by diabetes (29%). Our study corroborates with study done by Kavita Sharma et al.,[17] where the "Effectiveness-Based Guidelines for the Prevention of Coronary Artery Disease in Women—2011 Update" women were divided into 3 categories basing on their risk score i.e.: 1) high risk; 2) at risk; and 3) optimal risks.[18] Women with known CAD, peripheral arterial disease, symptomatic carotid artery disease, abdominal
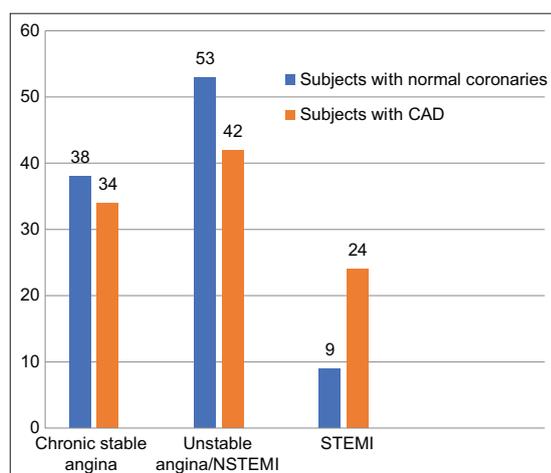

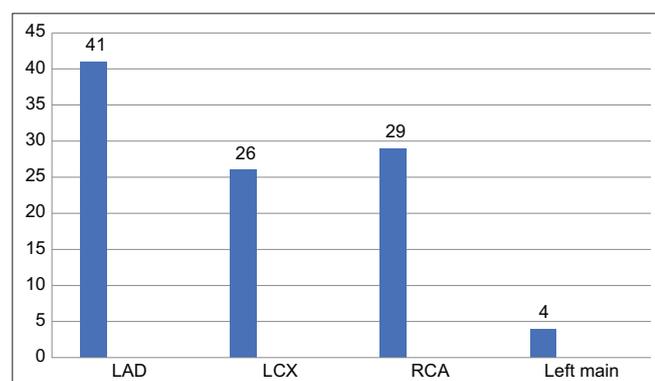**Figure 3:** Type of presentation in patients with normal coronaries Vs patients with CAD

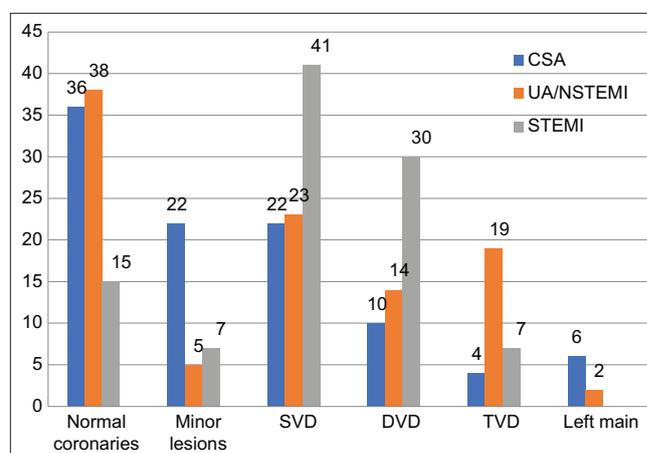**Figure 4:** Angiographic profile in women with CAD.

Figure 5: Relation of type of presentation with type of lesion

aortic aneurysm, end-stage or chronic kidney disease were considered as high risk category. Whereas cigarette smoking, systolic blood pressure ≥120 mm Hg, diastolic blood pressure ≥80 mm Hg, or treated hypertension, total cholesterol >200 mg/dl, HDL cholesterol <50, or treated dyslipidemia, obesity, poor diet, physical inactivity, family history of premature CAD occurring in first-degree relatives in women <65 years of age, metabolic syndrome, evidence of advanced subclinical atherosclerosis (e.g., coronary calcification, carotid plaque, or thickened intima-media thickness) poor exercise capacity on treadmill test and/or abnormal heart rate recovery after stopping exercise, lupus or rheumatoid arthritis or history of pre-eclampsia, gestational diabetes, or pregnancy-induced hypertension were include as at risk status. Optimal risk is defined as having all of the following factor i.e. total cholesterol <200 mg/dl (untreated), blood pressure <120/80 mm Hg, fasting blood glucose <100 mg/dl (untreated), body mass index <25 kg/m2, abstinence from smoking. Women with hypertension19 and diabetes,20 elevated triglycerides are greater risk factor for CAD in women versus men. Of the 323 women enrolled in the WISE-CVD cohort study21 who had suspected ischemic chest pain, age, hypertension, diabetes mellitus, prior MI, current hormone replacement therapy and unstable angina are all significant independent predictors of presence of significant coronary artery disease (p<0.05). In a similar study by Farshid Gheisari,22 older age, higher blood pressure, diabetes mellitus, previous h/o premature CAD, hyperlipidaemia were significantly associated with CAD in the female population. The higher levels of systolic and diastolic blood pressures, along with older age, were a significant risk factor in women (P < 0.05). Previous h/o premature CAD, diabetes mellitus, hypertension and hyperlipidemia, had a strong correlation with CAD in our female population. According to that study the most effective factor for women was previous h/o ischemic heart disease. Olivia Manfrini9 found current smoking and diabetes disproportionately increased the risk of CAD in women. Also studies by Afsana Rahman, MST, Nurun Naher23 on "risk factor analysis of MI in females" showed hypertension, diabetes mellitus, low HDL high cholesterol, tobacco use and family h/o CAD were the most commonly associated risk factors in females with CAD. Jonathan C. Brown; Thomas E24 also found similar results i.e. hypertension, hyperlipidaemia, diabetes, obesity, family h/o premature CAD etc were the attributable risk factors for development of CAD. Out of 140 patients, 45 (32%) had normal coronaries while 95(68%) had coronary lesions on angiography (Figure 3). The angiographic profile of women undergoing coronary angiogram (Figure 4) showed most commonly vessel to be involved was left anterior descending coronary artery (LAD) in 78 (41%) women followed by right coronary artery (RCA) in 56

(29%) women, left circumflex coronary artery (LCX) in 50 (26%) and LMCA in 8 (4%) women. This similar pattern of involvement of coronary arteries was seen in Babu Ezhumalai and Balachander Jayaraman et al.,25 where angiographic distribution of 500 patients showed involvement of LAD in 176 (35.2%) women, LCX in 128 (25.6%) women, RCA in 130 (26%) women and LMCA in 17 (3.4%) women. LAD was the most common vessel involved followed by almost equal prevalence of LCX and RCA. LMCA was the least affected vessel. Similar pattern was also observed in study done by Lu Yihua et al.26 In our study, among premenopausal women 13 (62%) had CAD on coronary angiography and 8 had normal coronaries which corroborates with the previous studies done by Lu Yihua et al.,26 where 82.46% of premenopausal patients identified as ACS. One of the largest reports of angiographic findings in young patients with CAD comes from a sub study of the CASS trial. et al.27 This trial concluded that young women had a higher frequency of angiographically normal coronary arteries than young men and single vessel coronary disease was more common (24%) as compared to triple vessel disease (39%). Similar finding observed by Pathak where the analysis of coronary angiographic findings showed that women most commonly suffered from single vessel disease (51%) followed by triple vessel disease (27%), double vessel disease (07%). Normal coronaries found to be in 15% of women undergoing coronary angiograph HDL ≤40mg/dl and hypertension were the most common risk factors 8 (62%) followed by TG ≥150 mg/dl(46%). Diabetes was present in 5 patients (38%).

The prevalence of cardiac risk factors and the rate of angiographically critical CAD in women under the age of 45 years for first time evaluation of chest pain were studied by De S et al.28 When compared with people without angiographic evidence of CAD, women with CAD had a higher prevalence of dyslipidemia (72% vs 47%, p=0.002), diabetes (29% vs 9%; p<0.001) and smoking (67%vs 50%; p=0.03). The association of risk factors with angiographically proven coronary artery disease was estimated in our study. The relationship between diabetes (p=0.009), BMI >25kg/m² p=0.0070, family history of premature CAD (p=0.006), total cholesterol >200mg/dl (p=0.011), LDL >100mg/dl (p=0.006) and HDL<40mg/dl (p=0.009) was found to be statistically significant. Similar findings were reported by Kunal Mahajan where the risk factors present in triple vessel disease were analyse d.Triple vessel disease, was more in those with diabetes mellitus (p=0.0231), total cholesterol >200mg/dl (p=0.007), LDL >100mg/dl (p=0.002) and TG >150mg/dl (p=0.047). This relation was statistical significant.29 Out of 45 patients with normal coronaries, 53% (24 patients) presented with unstable angina/NSTEMI, 38% (17 patients) with chronic stable angina and 9% (4) with STEMI. Among 95

Table 1: Relationship of risk factors with coronary artery disease

Risk factors	Total no	Coronary artery disease		P value
		Present	Absent	
Diabetes	45	39	6	0.009*
Without Diabetes	95	56	39	
Hypertension	71	55	16	0.058
Without Hypertension	69	40	29	
Passive smoking	20	16	4	0.301
Without Passive smoking	120	79	41	
Family h/o premature CAD	19	18	1	0.006*
NoFamily h/o premature CAD	121	77	44	
Tobacco chewing	19	17	2	0.304
Without tobacco chewing	121	78	43	
BMI≥25kg/m2	24	22	2	0.007*
BMI<25kg/m2	116	73	43	
Total cholesterol ≥200mg/dl	35	30	5	0.011*
Total cholesterol<200mg/dl	105	65	40	
LDL≥100mg/dl	44	37	7	0.006*
LDL<100mg/dl	96	58	38	
HDL≤40mg/dl	33	31	2	0.009*
HDL>40mg/dl	107	64	43	
TG≥150mg/dl	40	31	9	0.161
TG<150mg/dl	100	64	36	
Post-menopausal	119	82	37	0.613
Premenopausal	21	13	8	

*- statistically significant

Table 2: Correlation of patients with triple vessel disease and type of presentation

	Total no	Triple vessel Disease		P value
		Present	Absent	
Chronic stable angina	32	2	30	
Not presenting with Chronic stable angina	53	14	39	0.079
UA/NSTEMI	40	12	28	
Not presenting with unstable angina/NSTEMI	55	4	51	0.011
STEMI	23	2	21	
Not presenting with STEMI	72	14	58	0.22

Triple vessel disease patients presented more with unstable angina/NSTEMI (p=0.011) which is statistically significant.

patients with coronary artery disease, 42% (40) presented with unstable angina/NSTEMI, 34% (32) with chronic stable angina and 24% (23) with STEMI. In a similar study conducted by Pathak,[30] retrospective analysis of the presenting complains found that most common indication to perform angiography was unstable angina/NSTEMI (51%) followed by Stable Angina (25%) and Myocardial infarction/STEMI (13%). Similarly findings observed by Davis,[31] out of 101 consecutive female patients significant coronary artery disease was unstable angina (64.3%) followed by stable angina (24.3%), myocardial infarction (4.3%) and atypical chest pain in 2.8%. In normal coronaries half the patients presented with atypical chest. In patients with CAD, 16(17%) had minor lesions. Majority had significant lesions in the form of single vessel disease (37pts, 39%), double vessel disease (22pts, 23%), triple vessel disease (16pts, 17%) and left main disease (4%). So, single vessel disease was found to be most common pattern of coronary lesion. In the analysis of coronary angiogram from a large

series of women enrolled in WISE study, of those with significant CAD, most had multi vessel disease. Single vessel disease was the most common pattern followed by double vessel disease. Left anterior descending artery was most commonly involved vessel followed by right coronary artery. Similar finding was observed by Pathak[16] where the commonest pattern was single vessel disease (51%) followed by triple vessel disease (27%) and then, double vessel disease (07%). Normal coronaries found to be in 15% of women undergoing coronary angiography. In a study by Jorge Gajardo-Navarrete et al.,[32] absence of coronary lesions was found in 44 and 32% of premenopausal and postmenopausal women, respectively (p < 0.01). Premenopausal women with T2DM had a higher frequency of multi-vessel disease than those without the disease (25 and 4.5%, p < 0.001). The frequency of multi-vessel disease was higher in postmenopausal than premenopausal women (24 and 11%, p < 0.01). Hypertension, T2DM and renal involvement were associated with a higher frequency multiple vessel disease.

Table 3: Correlation of patients with triple vessel disease and risk factors

Risk factors	Total no	Triple vessel disease		P value
		Present	Absent	
Diabetes	39	11	28	
Without Diabetes	56	5	51	0.0231
Hypertension	55	9	44	
without Hypertension	40	7	35	1
Passive smoking	16	1	15	
Without Passive smoking	79	15	64	0.292
Family h/o premature CAD	18	3	15	
Without Family h/o premature CAD	77	13	64	1
Tobacco chewing	17	3	14	
WithoutTobacco chewing	78	13	65	1
BMI≥25kg/m2	22	3	19	
BMI<25kg/m2	73	13	60	0.751
Total cholesterol≥200mg/dl	30	10	20	
Total cholesterol<200mg/dl	65	6	59	0.007
LDL≥100mg/dl	37	12	25	
LDL<100mg/dl	58	4	54	0.002
HDL≤40mg/dl	31	7	24	
HDL>40mg/dl	64	9	51	0.394
TG≥150mg/dl	31	9	22	
TG<150mg/dl	64	7	53	0.047

Triple vessel disease was more commonly associated with diabetes (p=0.0231), total cholesterol ≥200mg/dl (p=0.007). LDL ≥100mg/dl (p=0.002) and TG ≥150mg/dl (p=0.047). This relation was statistically significant.

CONCLUSION

In our study, incidence of CAD is higher as the age advances and more common among postmenopausal as compared to premenopausal women. Most common presentation was unstable angina/NSTEMI. A substantial percentage of women presenting with symptoms of anginal pain had angiographically normal coronaries. So it is evident that angina as presenting symptom is less predictive of occlusive CAD in women. Among premenopausal women with CAD, hypertension and low HDL are the most common risk factors. In women with CAD, majority had single vessel disease with LAD was the most commonly involved vessel. Diabetes mellitus and BMI ≥25kg/m2, family history of premature CAD, elevated total cholesterol and LDL, low HDL are significantly associated with angiographically proven CAD in women. Women with triple vessel disease are more likely to present with unstable angina and associated with elevated total cholesterol, elevated LDL and elevated triglycerides.

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