PREDICTORS OF RISK FOR CORONARY ARTERY LESIONS IN WOMEN WITH SYMPTOMS OF CORONARY ARTERY DISEASE

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ABSTRACT

BACKGROUND

Coronary artery disease is a leading cause of mortality and morbidity in the world. Women differ from men with regard to coronary artery disease in presentation, risk factors, prognosis and in acceptance of secondary prevention modalities. With regard to presentation, most of the women with coronary artery disease present at a later age.

MATERIALS AND METHODS

Female patients with STEMI, NSTEMI or chronic stable angina without significant comorbidities were studied and results were analysed.

RESULTS

140 subjects were included in the study. The mean age of patients was 54.19±9.89 years, maximum number of patients were >60 yrs. of age. 21 (15%) were premenopausal and rest 119 (85%) were postmenopausal. 95 (68%) patients had angiographic evidence of CAD while coronary angiography was normal in 45 (32%) patients. Total cholesterol, LDL, HDL were found to be significant from bivariable analysis, but in multivariable analysis, single independent predictor of a lesion in the coronary arteries was found to be HDL cholesterol with adjusted risk ratio of 1.3 (1.1-1.5).

CONCLUSION

Women with acute coronary syndromes present more with unstable angina/NSTEMI. Women are less likely to present with the syndrome associated with occlusive thrombus- that is, with infarction with ST elevation. Family history of premature coronary artery disease is an important risk factor in women.

Total cholesterol, LDL, HDL were found to be significant from bivariable analysis, but in multivariable analysis, single independent predictor of a lesion in the coronary arteries was found to be HDL cholesterol.

KEYWORDS

Coronary Artery Lesion, Coronary Artery Disease, Predictors, Risk, Women.

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BACKGROUND

Coronary artery disease is a leading cause of mortality and morbidity in the world. Women differ from men in their clinical presentation and profile. More women constitute the cases in >65 years age category. More women die of the disease than men in this age group. Women with acute ischemic syndromes tend to be older than men. They also have more chance of having risk factors like hypertension, diabetes, angina and congestive heart failure.[1]

Coronary artery disease is now the commonest cause of death in women in many countries. Its incidence increases with age, rising rapidly after menopause by 65 years. The proportion of older women increasing, the incidence of cardiovascular disease is bound to increase. Before the age of 65, coronary artery disease is half as common in women than in men, affecting one in nine women aged 45 to 64. But a quarter of deaths from myocardial infarction in women under 65 occur in the less than 45 age group.[2-4]

Women differ from men with coronary artery disease in presentation, risk factors, prognosis and in acceptance of secondary prevention modalities.[5-8] With regard to presentation, most of the women with coronary artery disease presents at a later age.[9] Typical angina being less predictive of coronary artery disease, they may present with shoulder or jaw pain, dyspnoea or nausea. As regarding the risk factors, diabetes has a stronger influence on women, and they tend to have lesser levels of the HDL cholesterol described to be protective against coronary artery disease. The risk of coronary artery disease increases after menopause as well. With regard to prognosis, women tend to die more likely after a first myocardial infarction or experience more long-term disability.[5]

Aim of the Study

To find the risk factors of coronary artery lesions in women presenting with symptoms of coronary artery disease.

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MATERIALS AND METHODS

Female patients with STEMI, NSTEMI or chronic stable angina without significant comorbidities were studied after Institutional Committee approval and informed consent from subjects and results were analysed.

Design – Cohort study.

Setting – Lok Manya Tilak Municipal Medical College, Sion, Mumbai, a tertiary care hospital.

Period – Jan 2005 to July 2006.

Sample Size – The sample size was fixed as 140 patients.

Inclusion Criteria

1) Female patients with acute ST elevation myocardial infarction by standard definition.
   a) Characteristic chest pain suggestive of ischemia for prolonged period (>30 min).
      OR
   b) Evolutionary changes in ECG showing ST elevation of atleast 1 mm in two contiguous limb leads or 2 mm in two contiguous chest /precordial leads.
      OR
   c) Characteristic rise and fall of enzymes (CK-MB and Troponins) suggestive of myonecrosis.
2) Female patients presenting with unstable angina /NSTEMI. Unstable angina is defined as angina with atleast one of the following.
   a) Occurring at rest (or minimal exertion) and usually lasting more than 20 min.
   b) Being severe and described as frank pain and of new onset (i.e. within a month).
   c) Occurring after a crescendo pattern.
      Patients with elevated biomarkers of cardiac necrosis (CPK MB, Troponin) are diagnosed as having NSTEMI.
3) Female patients with chronic stable angina.
   a) Typical angina
      * Substernal chest discomfort with a characteristic quality and duration that is
      -Provoked by exertion or emotional stress and
      - Relieved by rest or nitroglycerine
   b) Atypical angina (probable) meeting 2 of the above characteristics.
   c) Who had other standard indications for coronary angiography?

Proven cases of coronary artery disease-

Following angiography, any lesion less than 70 percent was taken as a minor lesion for the purpose of calculation and greater than or equal to 70 percent were considered significant. Significant lesions were further typed as single vessel disease, double vessel disease and triple vessel disease. The patients were noted as if having left main vessel disease too.

Exclusion Criteria

Patients with serious comorbidities in whom the risks of angiography outweigh the benefit of the procedure.

Data Collection

The subjects were recruited after getting informed written consent and demographic data clinical features, risk factors laboratory and angiographic profile entered using a proforma. Coronary angiography was performed on SIEMENS Image Intensifier Based Cathlab System in the department. It was performed in multiple projections by the Judkins technique using either femoral or trans radial approach, Images were acquired on cine films and stored in hi-cor system.

Angiograms were analysed from cine recording and reports were compared with QCA measurements for extent of stenosis. Presence, location and extent of CAD were noted. For the purpose of study, significant stenosis CAD was defined as luminal stenosis more than 70%. Patients with less than 70% luminal stenosis was defined as having minor lesions. Patients were classified as single vessel disease if only one vessel had significant stenosis, double vessel disease if two vessels were involved and triple vessel disease if 3 vessels were involved. If there was a significant left main disease, it was considered to have left main disease. The risk factors of the patients were entered using a proforma and the significance in causation of coronary artery disease was analysed.

Statistical Analysis

Qualitative variables are described as percentages and quantitative as means with Standard deviation. Chi- square test was done for bivariable analysis of qualitative variables and independent sample t- test for quantitative variables. Relative risk with the 95% confidence interval has been computed. Multivariable analysis was done using logistic regression.

RESULTS

140 subjects were included in the study. The mean age of patients was 54.19±9.89 years, maximum number of patients were >60 yrs. 21(15%) were premenopausal and rest 119(85%) were postmenopausal. 95(68%) patients had angiographic evidence of CAD while coronary angiography was normal in 45 (32%) patients.

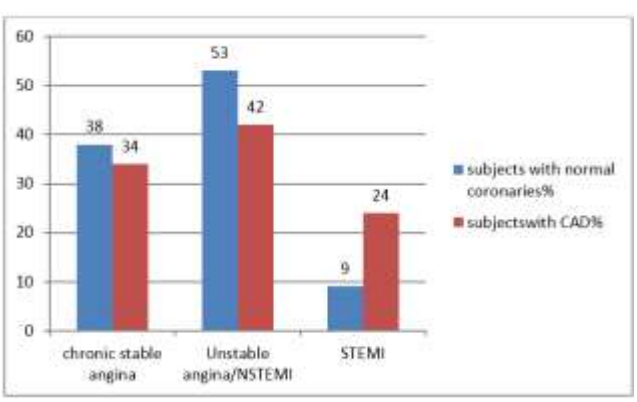

Figure 1. Type of Presentation in Patients with Normal Coronaries and Patients with CAD

Coronary vessel	No (n=192)	%
LAD*	78	41
LCX†	50	26
RCA‡	56	29
Left main	8	4

Table 1. Distribution of Lesions in Coronary Vessels

*LAD-left anterior descending, †LCX-left circumflex, ‡RCA –right coronary artery

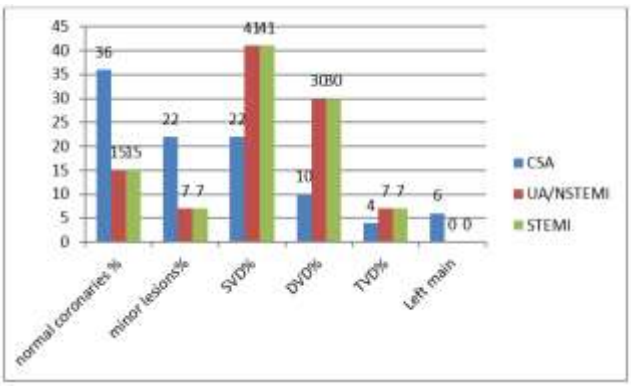

Figure 2. Relation of Type of Presentation with Type of Coronary Lesion

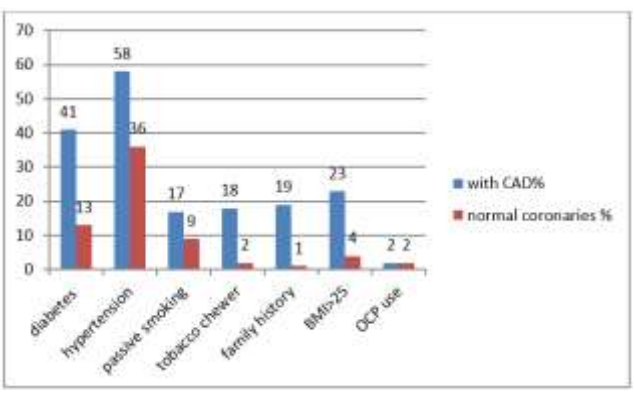

Figure 3. Risk Factor Distribution in Patients with and without Coronary Artery Lesion

	Coronary Lesion Present	Coronary Lesion Absent	Relative Risk (95% CI of RR)
Diabetic	39 (86.7%)	6 (13.3%)	1.5 (1.2-1.8)
Hypertension	53 (75.7%)	17 (24.3%)	1.3 (1.0-1.7)
Passive smoking	15 (71.4%)	6 (28.6%)	1.1 (0.8-1.5)
Tobacco	17 (89.5%)	2 (10.5%)	1.4 (1.2-1.8)
Family history	18 (94.7%)	1 (5.3%)	1.5 (1.3-1.8)
OCP use	2 (66.7)	1 (33.3%)	1.0 (0.4-2.3)
Premenopausal	12 (57.1%)	9 (42.9%)	0.8 (0.6-1.2)
Obesity	22 (91.7%)	2 (8.3%)	1.5 (1.2-1.8)
Stable angina	32 (65.3%)	17 (34.7%)	0.9 (0.7-1.3)
Unstable angina	38 (59.4%)	26 (40.6%)	0.8 (0.6-1.0)
STEMI	23 (85.2%)	4 (14.8%)	1.4 (1.1-1.7)

Table 2. Risk Factors and Prediction of Risk for Lesion in Angiography

	1-Coronary Lesion Present 2-Coronary Lesion Absent	N	Mean	Std. Deviation	Std. Error Mean	P Value *
Age	1	93	55.68	9.209	0.955	0.007
	2	47	50.96	10.644	1.553	
BMI (kg/m^2)	1	93	23.14	2.253	0.234	0.000
	2	47	21.55	1.626	0.237	
total cholesterol	1	93	181.94	29.823	3.092	0.007
	2	47	167.89	25.670	3.744	
LDL	1	93	110.04	27.740	2.877	0.001
	2	47	93.34	23.951	3.494	
HDL	1	93	41.71	3.838	0.398	0.000
	2	47	48.53	5.683	0.829	
TG	1	93	148.78	29.333	3.042	0.000
	2	47	127.87	30.748	4.485	

Table 3. Relationship of Risk Factors with Coronary Artery Lesion

*t- test.

Mean Age, BMI, Total cholesterol, LDL and TG value were significantly higher in those with lesions in angiogram and HDL was significantly lower.

	Coronary Artery Lesion Present (n= 95)		Coronary Artery Lesion Absent (n= 45)			
	n	%	n	%	Odds Ratio	95% CI of OR
Total Cholesterol >/= 200 mg% (n=35)	30	31	5	13	3.69	1.23-11.86
LDL >/= 100 mg% (n= 34)	37	39	7	18	3.46	1.31-9.53
HDL </= 40 mg% (n= 34)	31	33	3	7	6.78	1.82-29.80
Triglycerides >/= 150 mg% (n= 40)	31	33	9	20	1.94	0.78-4.95

Table 4. Patients with Abnormal Lipid Values in those with Normal Coronaries and those with CAD

Lipid Profile (Mean)(mg/dl)	Subjects with CAD Mean (SD)	Subjects with Normal Coronaries Mean (SD)
Total Cholesterol	181.83 (30.39)	165.23 ± 20.38
LDL	110.68 ± 28.47	91.73 ± 20.08
HDL	41.74 ± 3.86	48.89 ± 5.53
Triglycerides	150.16 ± 30.46	124.13 ± 25.31

Table 5. Independent Risk Factors of Coronary Artery Lesion after Multivariable Analysis

	p-value	Adjusted Risk	Lower Limit of 95% CI Adjusted Risk	Upper Limit of 95% CI Adjusted Risk
Age	0.202	0.968	0.922	1.017
Diabetes	0.243	0.460	0.125	1.691
Hypertension	0.152	0.469	0.166	1.323
Tobacco Chewing	0.066	0.180	0.029	1.119
Family History	0.099	0.141	0.014	1.448
STEMI	0.124	0.303	0.066	1.390
Total Cholesterol	0.095	1.047	0.992	1.106
LDL	0.315	0.972	0.919	1.028
HDL	0.001	1.307	1.123	1.521
TG	0.265	0.985	0.960	1.011
Obesity	0.134	0.245	0.039	1.540
Constant	0.007	0.000		

Table 6. Single Independent Predictor of a Lesion in the Coronary Arteries was HDL Cholesterol with Adjusted Risk Ratio of 1.3 (1.1-1.5)

DISCUSSION

This study was done to assess the clinical and risk factor profile of women admitted with coronary artery disease and to analyse the correlation of angiographic findings in relation to risk factors.

The mean age of affected group in the study was 54.19±9.89 years, maximum patients being in >60 years age group. Youngest patient was 30 years and oldest was 75. The mean age is in par with finding from many other studies. Women are about 10 years older than men at first manifestation of CAD in the absence of other risk factors.[1-8]

Postmenopausal women predominated in numbers in this study 119 (85%).

Out of 140 patients, 45(32%) had normal coronaries while 95(68%) had coronary lesions on angiography. This is similar to the 30.7% normal coronaries as concluded by Dave TH et al after analysing a similar set of 101 female patients.[10] In the WISE study, women enrolled with suspected ischemic chest pain, 34% had no detectable coronary lesion. This was a large series analysis of coronary angiogram in symptomatic women. This result is attributable to atypical chest pain in women.

Out of 21 premenopausal females, 13(62%) had evidence of coronary artery disease on angiography, of which 48% had significant coronary artery disease. In a study of women under the age of 45 years referred for coronary angiography, De S et al found that 65% had completely normal coronary arteries.[11]

Of the 323 women enrolled in the pilot phase of Women's Ischemia Syndrome Evaluation study who had suspected ischemic chest pain, age, hypertension, diabetes mellitus, prior myocardial infarction, current hormone replacement therapy, and unstable angina were all significant, independent predictors of significant disease.[12,13]

Numerous epidemiological studies have shown that the presence of hypertension increases the risk of CAD, not only in at-risk populations, but also in general population. Hypertension confers a 4-fold risk of CAD in women versus a 3-fold one in men. Women with hypertension experience a risk of developing CAD that is 3.5 times that of female controls with normal blood pressure. The systolic blood pressure continues to increase disproportionately in women until the age of 80. Hypertension was the commonest risk factor found in this study.[14,15]

Gurewitz O et al studied the clinical profile, angiographic results, and long term follow up of 135 women[16] aged less than or equal to 50 years referred for coronary angiography because of chest pain. The most prominent risk factor was hyperlipidaemia (60%), followed by a family history of premature coronary artery disease (44%), systemic hypertension (40%), cigarette smoking (31%), postmenopausal state (23%), and diabetes mellitus (21%). Women with CAD compared to those without significant CAD had a higher prevalence of hyperlipidaemia (71% vs. 45%; p=0.002) and postmenopausal state (30% vs. 16%; p=0.028).

Clinical and risk factor profile of 101 consecutive female patients subjected to coronary angiography was analysed by Dave TH et al.[10] Risk factor profile in patients with angiographically proven coronary artery disease in their study included hypertension in 52.9%, diabetes mellitus in 44.3%, postmenopausal state in 84.3%, positive family history in 51.4%, obesity in 58.3% and smoking in 4.3%. Risk factors in 31 patients with normal coronaries included hypertension in 29%, diabetes mellitus in 6.5%, positive family history in 45.2%, obesity in 45.2%, postmenopausal state in 48.4% and smoking in none. In the present study also, hypertension topped the list of risk factors by number percentages, followed by diabetes mellitus in patients with angiographically evident coronary artery disease.

The prevalence of cardiac risk factors and the rate of angiographically critical coronary artery disease in women under the age of 45 years for the first time evaluation of chest pain was studied by De S et al.[11] When compared to people without angiographic evidence of CAD, women with CAD had a higher prevalence of dyslipidaemia (72% versus 47%, p=0.002), diabetes (29% versus 9%, p<0.001) and smoking (67% versus 50%, p=0.03).The association of risk factors with angiographically proven coronary artery disease was analysed in this study. The relationship between diabetes (p=0.009), BMI >/=25 (P=0.007), family history of premature CAD (P=0.006), total cholesterol >/=200(p=0.011), LDL./=100 (p=0.006) and HDL </=40(P=0.009) were found to be statistically significant as in other studies studying these risk factors and their relation to coronary artery disease.[17-21]

In the study by De S et al to determine the rate of angiographically critical coronary artery disease in women under the age of 45 years who sent for the first –time evaluation of chest pain requiring cardiac catheterisation, 52 percent patients with significant coronary artery disease had single vessel disease.[11] In the present study, single vessel disease was commonest followed by double vessel disease as well.

Left anterior descending (41%) was the most common vessel followed by right coronary artery (29%). The LAD was the most commonly affected as per study by Pinto RJ et al as well.[13] Among patients with TVD, 75% (12 out of 16) presented with unstable angina /STEMI. This relation was found to be statistically significant.

CONCLUSION

Women with acute coronary syndromes present more with unstable angina/NSTEMI. Women are less likely to present with the syndrome associated with occlusive thrombus- that is, with infarction with ST elevation.

Among premenopausal women with coronary artery disease, hypertension and low HDL are the most common risk factors.

Diabetes mellitus and body mass index more than or equal to 25 are significantly associated with angiographically proven coronary artery disease in women.

Family history of premature coronary artery disease is an important risk factor in women. Total cholesterol, LDL, HDL were found to be significant from bivariable analysis, but in multivariable analysis, single independent predictor of a lesion in the coronary arteries was found to be HDL cholesterol with adjusted risk ratio of 1.3 (1.1-1.5).

Elevated total cholesterol and LDL and decreased HDL is significantly associated with coronary artery disease in women. However, relation with elevated triglycerides is not statistically significant

Women with triple vessel disease are more likely to present with unstable angina.

Triple vessel disease is more common in women with diabetes mellitus, elevated total cholesterol, elevated LDL and elevated triglyceride levels.

Limitations of the Study-

Sample size being small, broad conclusions can't be made from the study.

The effect of various risk factors on disease progression was not studied as no follow up was done as part of study.

Premenopausal patients formed only a small group in the study.

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