# Clinical Features and Angiographic Findings in Premature Coronary Artery Disease; Comparison Between Males and Females

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**Introduction:** Coronary artery disease has emerged as one of the leading causes of premature mortality and morbidity in South Asians. In contrast to males, younger women are ignored due to prevailed social trends. Better characterization of disease presentation in this group will help us in formulating adequate management policies.

**Objectives:** To study clinical features, risk factors and angiographic findings in female patients with premature Ischemic heart disease comparing with men of similar age.

**Study design:** It was Interventional:Quasi experimental study.

**Setting:** Punjab Institute of Cardiology Lahore.

**Duration:** From 19th of January 2002 till 27th of September 2003.

**Subjects and methods:** 100 female patients and 100 male patients age 50 or below were studied, who were referred for coronary angiography. Patients with previous coronary angiogram or revascularization were excluded. Data was collected over prescribed proforma and results analyzed.

**Results:** Prevalence of significant risk factors in women compared with men were hypertension, (50% vs 28%; P<0.01), hyperlipidemia (62% vs 26%; P<0.01) diabetes mellitus (46% vs 8%; P<0.01), sedentary life style (44% vs 24%; P<0.01) and obesity (58% vs 22%; P<0.01). Majority of women (84% vs 54%; P<0.01) presented with angina compared with men. No significant difference was noted in distribution of coronary artery disease between two sexes.

**Conclusion:** Women who developed premature coronary artery disease had significant prevalence of majority of conventional risk factors than their male counterparts and more likely to present with angina than myocardial infarction. However distribution and severity of coronary artery disease was similar between the two sexes.

**Key words:** Females coronary disease chest pain risk factors coronary angiography

## Introduction

Heart disease is the leading cause of death for women both in the developed and underdeveloped nations. Each year approximately 2.5 million U.S. women are hospitalized for cardiovascular illness, which also claims the lives of 500.000 women annually, half of these deaths are due to coronary artery disease.[1] Despite the magnitude of this problem, we have insufficient information about diagnostic, therapeutic, preventive strategies. This is due to lack of participation of women in research studies due to the exclusion of women of childbearing age and elderly aged women because of their frequent co-existing illnesses.[2-4]

Whereas cardiovascular deaths in the U.S. men have declined over past 2 to 3 decades, the number in women remains unchanged or is on the rise. According to AHA surveys of women's awareness, only 13% women have heard the heart disease is the leading cause of death among women. Firstly, women underestimate their risk of cardiovascular disease and lack awareness; secondly, data about women is lacking. The epidemiology of CAD clearly differs between the sexes, and there are further unique aspects to cardiac disease in women, such as issues related to hormones, pregnancy, and differing psychosocial factors.

Framingham data has described typical angina in women and myocardial infarction in men as first symp-tomatic presentation. The rate of early death after myocardial infarction is higher among women than men, even when coronary thrombolytic therapy is used, women who undergo coronary angioplasty, coronary or CABG, the in-hospital mortality is substantially higher than among men.

## Material and methods
### Setting
Punjab Institute of Cardiology, Lahore.

### Duration of Study
The study was conducted from 19th of January 2002 till 27th of September 2003 (Twenty months).

### Study Design
It was Interventional :Quasi experimental study.

### Sample Size
The study population was divided in to two groups.

**Group-I** comprising of 100 female patients.

**Group-II** comprising of 100 male patients.

Who were referred for coronary angiography.

### Inclusion Criteria
**1:** Patients aged 50 years or below.

**2:** Patients undergoing coronary angiography for the first time.

## Exclusion Criteria
**1:** All the patients aged more than 50 years.
**2:** Patients with previous coronary angiogram, Coronary Artery Bypass Graft Surgery or Coronary stent implantation were excluded from the study.

## Data Collection
After fulfilling the inclusion criteria, consent was taken and patient characteristics were recorded on a proforma, A full history was taken regarding the mode of presentation of chest pain, age, sex, occupation, address, history of smoking, diabetes mellitus, hypertension, family history of ischemic heart disease, use of contraceptives in women and their menstrual history, dietary habits, physical activity, socioeconomic status and life style. Obesity was defined as body mass index 27.8 and 27.3 for men and women respectively. Hypertension was defined as a systolic blood pressure more than 140 mm of Hg and a diastolic blood pressure of more than 90 mm of Hg in resting supine position, or current use of antihypertensive drugs. Cigarette smoking was ascertained for current and past use. Previous history of smoking was defined as total abstention for at least four week before admission. History of Diabetes Mellitus was considered to be present if the individual has been receiving insulin or oral hypoglycemics. Additional criteria included a fasting blood glucose level in excess of 125 mg/dl on two occasions. Positive family history was considered if premature CHD was present in first-degree relatives at age 55 year or younger in men and at age 65 year or younger in women respectively.

Coronary angiograms were classified in one of the following categories by visual assessment in two or more orthogonal views, angiographically normal arteries. Lumen irregularities or non-obstructive stenosis representing < 50% diameter reduction. Significant stenosis in one, two or three of the coronary arteries.

## Statistical Analysis
All the data was analyzed by SPSS Version 10.0 for Windows. These variables were analyzed by using simple descriptive statistics, using mean and standard deviation for quantitative data (age) and frequency, percentage for quailtative variables like risk factors (diabetes mellitus, hypertension, hyperlipidemia, smoking, obesity and family history of ischemic heart disease), clinical presentation (first presentation as angina or myocardial infarction, typical and atypical chest pain) and angiographic findings (single, two or three vessel disease). The relevant investigations were presented as positive and negative and were calculated as frequency and percentage.

The outcome variables were risk factors (diabetes mellitus, hypertension etc), clinical presentation (typical, atypical chest pain) and angiographic findings (single, two or three vessel disease). The two groups of gender were compared for outcome variables and any comparison found was statistically analyzed by using chi-square test as the data was mainly qualitative in nature, while continuous variable like age was compared between two groups by applying t-test. A p-value of equal to or less than 0.05 was considered as statistically significant.

## Results
A total of two hundred patients were studied comprising of hundred females and hundred males. Patient's demographics, clinical features and angiographic findings were recorded. Chi square test was applied for outcome variables to obtain p values. No subject was dropped out at any point in the study.

## Baseline Characteristics
The distribution of various conventional risk factors in women and men are presented in (Table 2). Diabetes mellitus, Hypertension, Hyperlipidemia, Obesity and Sedentary life style were a more common presentation in women compared with men. 58% of women with angiographically verified coronary artery disease had multiple conventional risk factors compared with 36% of men. Fewer women enrolled in this study were smokers compared with majority of men with an average daily consumption of more than 10 cigarettes for more than a decade of their life. A 24% of women were postmenopausal at time of enrolment in the study and 6% were on regular contraceptive use.

Majority of female patients belonged to middle and low income class and a small number were from high socioeconomic class compared with men (Table 3). A vast majority of female patients in middle and low income class were either uneducated or have hardly

**Table 1:** *Distribution of Risk Factors for Coronary Artery Disease Among Women and Men (Overlapping Risk factors).*

| RISK FACTORS | WOMEN Frequency (%) | | MEN Frequency (%) | | P-VALUE |
|---|---|---|---|---|---|
| Hypertension | 50 | *50.0* | *28* | 28.0 | <0.01 |
| Hyperlipidemia | 62 | *62.0* | *26* | 26.0 | <0.01 |
| Diabetes mellitus | 46 | 46.0 | 8 | 8.0 | <0.01 |
| Family History of CAD | 34 | 34.0 | 42 | 42.0 | =0.24 |
| Smoking | 8 | 8.0 | 56 | 56.0 | <0.01 |
| Sedentary life style | 44 | 44.0 | 24 | 24.0 | <0.01 |
| Obesity | 58 | 58.0 | 22 | 22.0 | <0.01 |

gone beyond matriculation while majority of men had education up to primary school level only. Mean age among women was 42.52 sd ± 4.22 while in men mean age was 37.34 sd ± 5.71 (p<0.01).

## Clinical Presentation

Angina was a common presentation in majority of women compared with men (84% vs 54%, p<0.01), out of which unstable angina was a more common feature in women. Differences in cardiovascular disease presentation in women and men are shown in (Table 2). Dyspnea was present in (34% vs 20%, p=0.03) of cases, postprandial chest symptoms (13% vs 14%), angina at rest (32% vs 16%) and chest pain on exertion was present in (44% vs 52%) of cases of women compared to men. 64% of the women presented with typical angina compared with 83% of men (p<0.01) and 26% had atypical angina compared with 9% of men (p<0.01), while non-specific symptoms were not statistically significant in the two groups. A presentation of myocardial infarction was a more prominent feature in men compared to women. Abnormal ECG at presentation was found in 66% of women and 70% of men.

### Coronary Angiographic Findings

Normal coronary arteries were seen in 10% of women and a further 10% had insignificant stenosis compared with 6% of men. Significant coronary artery disease on angiography was seen in 80% of women and 94% of men. Table 3 summarizes the distribution of various vessel involvement in both sexes.

Significant coronary artery disease associated with more than two conventional risk factors at a time was found in 58% of women compared with 36% of men (p<0.01) and 2% of women with diagnosis of myocardial infarction had normal coronaries compared to 6% of men. The extent of coronary artery disease in either sex is shown in (Figs. 1, 2). Angiographically verified significant coronary artery disease associated with typical angina was seen in vast majority of cases in both groups. Coronary ectasia was not seen in female patients enrolled in this study while it was found in 8% of male patients. Diffuse coronary artery disease involving one or more vessels was present in 10% of women compared with 8% of men. 88% of women had an ejection fraction >40% compared with 84% of men while ejection

**Table 2:** *Differences in Cardiovascular Disease Presentation Among Men and Women* (Overlapping Disease presentation).

| Disease presentation | Women | | Men | | P-Value |
|---|---|---|---|---|---|
| | Frequency n=100 | (%) | Frequency n=100 | (%) | |
| **Typical angina** | 64 | 64.0 | 83 | 83.0 | <0.01 |
| **Atypical angina** | 26 | 26.0 | 9 | 9.0 | <0.01 |
| **Non- specific** | 10 | 10.0 | 8 | 8.0 | =0.62 |
| **Myocardial infarction** | 16 | 16.0 | 46 | 46.0 | <0.01 |
| **Unstable angina** | 48 | 48.0 | 26 | 26.0 | <0.01 |
| **Stable angina** | 36 | 36.0 | 28 | 28.0 | =0.22 |
| **Dyspnea** | 34 | 34.0 | 20 | 20.0 | =0.03 |

**Table 3:** *Comparison of Distribution of Coronary Artery Disease Between Women and Men with Significant Stenosis.*

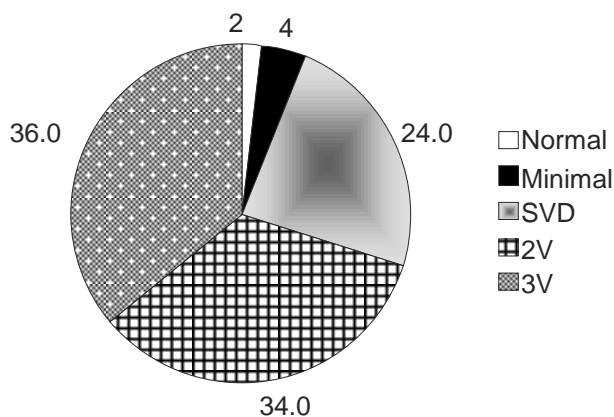| Coronary Artery Disease | Women | | Men | | P-value |
|---|---|---|---|---|---|
| | Frequency n = 80 | (%) | Frequency n = 94 | (%) | |
| **Single Vessel Disease** | 33 | 41.8 | 24 | 25.3 | = 0.02 |
| **Two Vessel Disease** | 24 | 30.4 | 34 | 36.2 | = 0.42 |
| **Three Vessel Disease** | 22 | 27.8 | 36 | 38.5 | = 0.15 |



**Figure 1:** *Extent of Coronary Artery Disease in Females of Study Population*

**Keys:**
SVD = Single Vessel Disease
2VD = Two Vessel Disease
3VD = Three Vessel Disease

fraction <40% was seen in 12% of women compared with 16% of men (p=0.42) on LV angiogram . Left main disease was seen in 4% of cases in either sex and one woman had an isolated left main disease which was not detected in any male patient included in the study, while the rest of the patients had other vessels involvement in addition to left main. Among patients with significant single vessel coronary artery disease proximal or mid LAD was involved in majority of cases in both sexes, LCX was comparatively more commonly involved in women and RCA in men (Figs. 3, 4, 5).
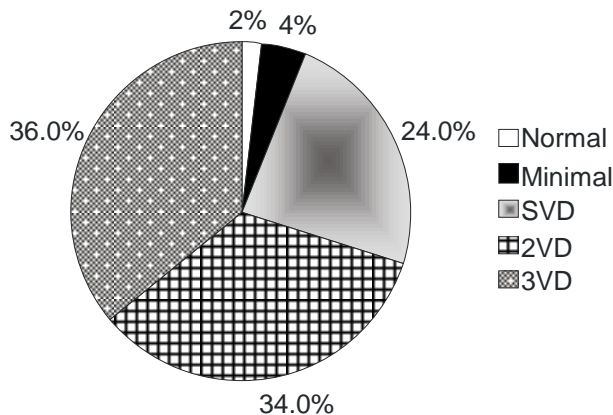


**Figure 2:** *Extent of Coronary Artery Disease In Men of Study Population*

**Keys:**

SVD = Single Vessel Disease

2VD = Two Vessel Disease
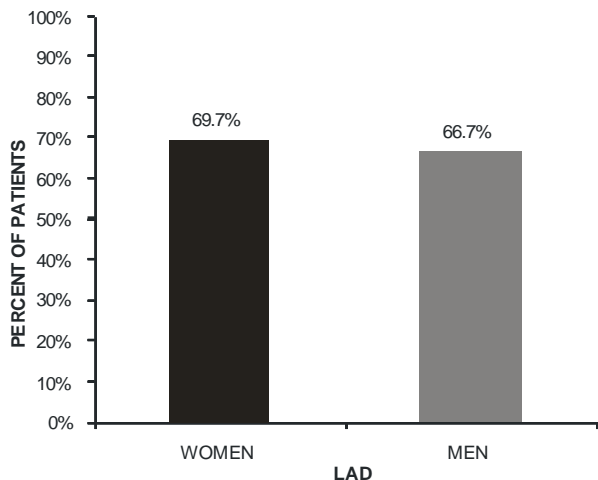
3VD = Three Vessel Disease



**Figure 3:** *Distribution of Involvement of Lad in Women And Men of Study Population with Significant Single Vessel Disease.*

RCA = Right Coronary Artery

KEY, LAD = Left Anterior Descending Artery

## Discussion:

In our study we have evaluated the prevalence of conventional risk factors, obesity and sedentary life style. Hypertension, hyperlipidemia, diabetes mellitus. and obesity were more common in female group than in males (Table 2). In addition, 24% of women were postmenopausal and 6% were on regular contraceptive use, rendering additional risk to women.
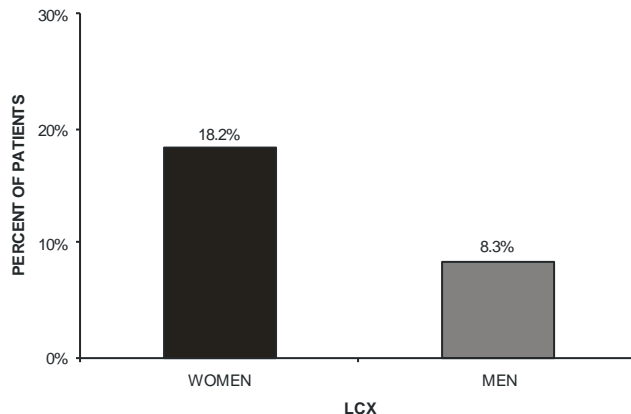


**Figure 4:** *Distribution of Involvement of LCX in Women and Men of Study Population With Significant Single Vessel Disease.*

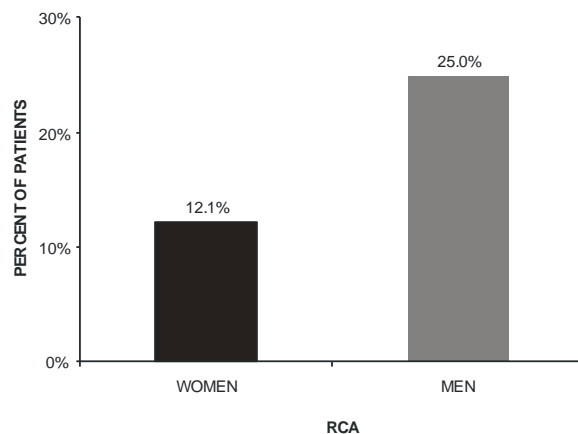LCX = Left Circumflex Artery

Key: LCX = Left Circumflex



**Figure 5:** *Distribution of Involvement of Rca In Women And Men of Study Population With Significant Single Vessel Disease*

KEY: RCA = Right Coronary Artery

Smoking was seen as a single common significant risk factor in men (P<0.01). Majority of women with obesity and conventional risk factors more then two at a time were associated with angiographically verified significant CAD compared with men (58% Vs 36%, P<0.01). It has been described in literature that women with CAD tend to have more co

morbidities than men. In our study 58% of the women with angiographically proven CAD had multiple risk factors.

M. Anis Memon, Abdus Samad[9] in their study on acute myocardial infarction in women has described a greater prevalence of hypertension (females 57%; males 27%), diabetes mellitus (females 34%; males 18%) and low prevalence of smoking among women (females 5%; males 60%).

In another study by Zubair Akram, M. Sarwar et al[10], the lipid abnormalities were the most common identifiable major risk factor in the female patient population and smoking was the most significant risk factor in the male group accounting for 45% of cases. Our study has also highlighted the relative importance of various risk factors for CAD in our young population. Smoking, as already described, which has emerged as a single large risk factor for acute myocardial infarction,[11] is associated with endothelial dysfunction and can precipitate coronary vasospasm. Thus smoking can contribute to myocardial infarction even in subjects with minimal atherosclerosis.

In one large case control study conducted in Karachi, Pakistan,[12] comprising 84.5% of males, to determine the risk factors for premature myocardial infarction among young South Asians, 51.8% were current smokers in the case group compared with 21.2% in the control group. This highlights the relative importance of smoking in the causation of premature CAD in younger male population, females being spared owing to very low prevalence of smoking in them in our society. Another study by Ambady Ramachandran, Immaneni Sathyamurthy et al,[14] has shown that general adiposity (BMI) is significantly and independently associated with CAD even after adjusting for age (P=0.003). In our study out of 58 percent obese women 86 percent had angiographically verified CAD.

The evaluation of the chest pain is a critical step in care of women with heart disease. It is a point at which women are likely to be treated differently from men,[18,19] especially when a diagnosis has not been established. Framingham data[5] has described angina in women and myocardial infarction in men as the first symptomatic presentation. In our study a large proportion of women 84% presented as angina compared with 54% of men, p<0.01 while diagnosis of myocardial infarction was made in only 16% of women compared with 46% of men (p<0.01).

Muhammad Anis Memon, Abdus Samad [9] had studied 1058 patients with definite evidence of first episode of AMI, 23% were women and 77% were men. So this aspect that women less commonly present with myocardial infarction and more commonly present with angina is consistent with studies local and abroad. In another study conducted in India, which analyzed CAD profile in 101 consecutive Indian women, 88.6% with angiographically verified CAD presented as angina, out of these unstable angina was in 64.3% and stable angina in 24.3%, myocardial infarction in 4.3% and atypical chest pain in 2.8%. In our study, the findings of clinical presentation of angina shown in (Table 2) closely correlates with study done in India differing in

large with atypical presentation of chest pain, which may be attributable to person to person variation in collecting history and patient perception/description of symptoms, that is largely affected by educational status and psychosocial aspects of that society. It has been described in various studies that atypical pain is more common in women than in men.[62,63] In our study 26% women presented with atypical symptoms compared with only 9% of men, P<0.01 (Table 2). On the contrary 83 percent of men presented with typical symptoms, so these findings clearly signifies the importance of atypical chest pain at presentation in women compared with men and warrants further evaluation for coronary artery disease in women presenting with atypical symptoms.

Definite angina is strongly suggestive of a significant CAD. In CASS[7] 62% of patients with definite angina had CAD. It has been shown previously that 90% of patients with typical symptoms will have coronary artery disease while the incidence of coronary artery disease in patients with atypical symptoms and asymptomatic patients is 50% and 4% respectively. In our study 84% of women with typical angina had significant CAD and it was 69% in atypical group. The prevalence of this relatively high incidence of coronary artery disease in our study is perhaps attributable to careful selection of patients for coronary angiography in our setup owing to various psychosocial and economic reasons. In WISE study[109] the significant coronary artery disease was found in 43% of women, of these, 43% had single vessel disease, 26% had two vessel disease and 31% had three vessel disease. In one study by M. Nawaz Lashari, Asadullah Kundi, et al[17] that described coronary angiographic findings in stable angina pectoris, irrespective of age and sex, as normal vessels 16%, single vessel disease 23%, two vessel disease 24% and three vessel disease 37%. In our study which included patients of younger age group (50 years or below) and which also focused on gender specific differences, the prevalence of various vessel involvement summarized in (Table 3) closely correlates with the National and International Studies. Moreover it is evident from above study data that significant coronary artery disease does not differ much amongst men and women. It has been described in literature that involvement of single vessel disease is more common in women than in men. In our study 33% of women had single vessel disease compared with 24% of men. The WISE study[16] has described an incidence of 62% significant stenosis in the proximal or mid LAD. In our study significant stenosis of LAD was seen in 69.70% of women compared with 66.70% of men (Fig. 3).

It has been emphasized in one study[17] that in Pakistan, 30% of all patients having coronary artery disease are below age of 40 years. In our study a large number of men (55%) and a small number of women (14%) were below the age of 40 years (P<0.01) and amongst this male group 59% were current smokers and only one female was smoker. This alarming high prevalence of coronary artery disease in young male group, especially current smokers, which signifies the importance of discouraging increasing smoking trends in

our youth. It has been described in literature that women tend to be older than men. In our study youngest man enrolled was 28 years and youngest woman 30 years of age and mean age amongst patients of study population was 42.52 in women and 37.34 in men (P<0.01).

## Conclusions

Women who develop premature coronary artery disease have significant prevalence of conventional risk factors in them as compared to their male counterparts except smoking which is less prevalent in Pakistani women. Women were more likely to present with angina than myocardial infarction. However distribution and severity of coronary artery disease was similar between the two sexes. Given the above mentioned findings, younger females with conventional risk factors should be carefully screened for presence or absence of coronary artery disease and given the same distribution and severity of coronary artery disease in both sexes, those females who are unfortunate enough to develop this complication, should be managed at par with their male counterparts.

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