A COMPARATIVE STUDY OF CORONARY ARTERY DISEASE IN PREMENOPAUSAL WITH POSTMENOPAUSAL WOMEN
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ABSTRACT: Coronary artery disease though more common in postmenopausal women, is not uncommon in premenopausal women especially in those having non-conventional risk factors.

MATERIALS & METHODS: All women who underwent coronary angiogram at the cardiac catheterisation laboratory at the department of cardiology, King George Hospital during the period between January 2014 and November 2014 were included in the study.

AIM OF THE STUDY: To know the severity of coronary artery disease in premenopausal women with postmenopausal women.

RESULTS: The incidence of single vessel disease and two-vessel disease is similar in both groups (22.4% and 24.6% in premenopausal and postmenopausal groups respectively. Postmenopausal women had more significant triple vessel involvement in 16.1% as compared to 8.0% in the premenopausal women.

CONCLUSION: Though severe form of coronary artery disease is observed in the postmenopausal women, significant coronary artery disease is also prevalent in premenopausal women.

KEYWORDS: Premenopausal, Postmenopausal, Coronary angiogram, Coronary artery disease.

INTRODUCTION: Coronary heart disease is the leading cause of death among postmenopausal women worldwide but it is a topic that has received inadequate attention. When premenopausal women get coronary artery disease the prognosis is poor. Post myocardial infarct mortality for women is higher than that for men for all ages and worse for younger women.¹ In the Framingham Heart Study, the one year mortality following myocardial infarction was 44% in women versus 27% in men.² Among women, the lifetime risk of death from coronary artery disease is more than 10 fold greater than that from breast cancer yet about 70% of educated women consider their risk of coronary artery disease (CAD) to be less than 1%.³ Recent data from National Health And Nutrition Surveys (NHANES) have shown that over the past two decades the prevalence of myocardial infarction has increased in midlife (35-54 years) in women, while declining in similarly aged men.⁴ In the Women's Ischaemia Syndrome Evaluation (WISE) study it was shown that young women with endogenous oestrogen deficiency have a more than sevenfold increase in coronary artery disease risk.⁵ In the Inter- heart study when compared to other participants, South Asians have a stronger association of hypertension, high waist hip ratio and adverse psychosocial factors with myocardial infarction.⁶ Among the non-traditional and newer risk factors for coronary heart disease are high levels of lipoprotein (a), Apo B, triglycerides and low density lipoprotein, low levels of high density lipoprotein and elevated plasma homocysteine, plasminogen activator-inhibitor and C-reactive protein.⁷,⁸ Women tend to have nonspecific electrocardiographic changes at rest, a lower exercise capacity and a smaller vessel size contributing to the lower sensitivity and specificity of non-invasive testing⁹ Microvascular
dysfunction and diffuse coronary atherosclerosis without obstructive lesions is more prevalent in women than in men.\textsuperscript{10,11} Coronary Angiogram is the most important diagnostic tool but women have more nonobstructive coronary artery disease. At younger ages women more often have acute coronary syndrome with angiographically normal coronary arteries than men. In the pilot phase of WISE study, 323 women were enrolled and 57\% of them had no significant CAD versus 43\% with significant CAD (stenosis more than 50\%) on coronary angiogram.\textsuperscript{12} In the Cholesterol And Recurrent Events (CARE) trial, the reduction in major adverse coronary events in women (46\%) was more than double that in men (20\%).\textsuperscript{13} The failure to treat women as vigorously as men contributes to their worse outcome although the gap is narrowing rapidly in western countries.\textsuperscript{14}

**AIMS AND OBJECTIVES:** To know the severity of coronary artery disease in premenopausal women in comparison with postmenopausal women.

**MATERIALS AND METHODS:** All women who underwent coronary angiogram for known or suspected coronary artery disease at King George Hospital, a tertiary care cardiac centre between January 2014 and November 2015 were included in the study after obtaining consent. All the cases were evaluated with detailed history, a resting electrocardiogram and echocardiography. Routine blood parameters including random blood sugar, serum creatinine were performed. Coronary angiogram was performed in all the cases (Siemens flat panel) in conventional views and modified views where necessary, to evaluate the left anterior descending, left circumflex and the right coronary arteries. The disease severity was assessed in individual vessels and their major branches by computerised quantitative coronary angiography (QCA) with the software in-built in the system. A significant coronary artery disease was defined as 70\% or more diameter stenosis of the involved artery. In case of left main coronary artery a diameter stenosis of 50\% and more was taken as significant stenosis. Baseline characteristics were calculated as mean ± standard deviation. The severity of the disease was evaluated as single vessel, 2 vessel, 3 vessel and left main involvement and the QCA evaluated diameter stenosis.

**RESULTS:** During the study period 348 women have undergone coronary angiogram of whom 125(35.9\%) patients were of premenopausal age. Postmenopausal women comprised of 223 (64.1\%) patients. These subjects included acute myocardial infarction, unstable angina and chronic stable angina the baseline characteristics are given in table 1. The mean age at presentation in the premenopausal women was 44.29 years. In the postmenopausal women the mean age at presentation to hospital was 61.04 years. The overall indication for coronary angiogram in both groups was unstable angina/non ST elevation myocardial infarction in 47.4\% of patients and ST elevation myocardial infarction in 32.7\% patients (Diagram 1).138 subjects had presented with features of unstable angina among whom the postmenopausal and premenopausal subjects were 72.5\% and 27.5\% respectively. The distribution of postmenopausal and premenopausal subjects in the 138 patients presenting with acute myocardial infarction was 66\% and 34\% respectively. 30 subjects had presented with symptoms of chronic stable angina of which the postmenopausal and the premenopausal subjects were 26.7\% and 73.3\% respectively.
Coronary angiography showed mild or insignificant coronary artery in 51.2% and 39.9% of subjects in premenopausal and postmenopausal groups respectively. The incidence of single vessel disease and two-vessel disease is similar in both premenopausal and postmenopausal groups (22.4% and 24.6%). Postmenopausal women had more significant triple vessel involvement in 16.1% as compared to 8.0% in the premenopausal subjects. (Diagram 3)

**DISCUSSION:** The gender specific difference in cardiovascular disease morbidity and mortality suggests lack of comparable progress in population based risk reduction efforts in women. Since 1984 the total number of deaths from cardiovascular disease has been greater for women when compared with men.15

Women tend to have increased early mortality following myocardial infarction. Due to age factor presentation and unfavourable risk factors. In the long run however, when differences in age and other risk factors are controlled for, women tend to have a better survival than men.16 It was reported that between 1990 and 2020 coronary artery disease mortality would increase by 29 percent in women and 48 percent in men in developed countries. The mortality estimates due to coronary artery disease for developing countries were 120 percent in women and 137 percent in men.17

In the present study patients who have presented to hospital with proven myocardial infarction were predominantly postmenopausal. However among women who underwent coronary angiogram premenopausal women accounted for 35.9%. This bias could be due to more frequent presentation of premenopausal subjects with symptoms of chronic stable angina which did not require hospitalisation. The prevalence of obstructive coronary artery disease is relatively low before menopause.18 There was a higher incidence of diabetes in postmenopausal women which in turn had translated in to more severe disease in the postmenopausal subjects. Presentation with acute coronary events was nearly similar in both groups. However a small Asian study by Saleh AU et al have shown a predominance of premenopausal women among patients presenting with ST elevation myocardial infarction.19 Severe coronary artery disease including two-vessel disease and triple vessel disease was more commonly seen among postmenopausal subjects. Data from Coronary Artery Surgical Study (CASS) Registry showed that many women with chest pain clinically indistinguishable from angina pectoris had no significant coronary artery disease in coronary angiography with 50% showing insignificant coronary occlusion.20 In the present study also there was a significant number of women who presented with coronary symptoms but had insignificant lesion on coronary angiography. Significant increase in risk factors like diabetes and hypertension play an important role in the higher incidence of severe coronary artery disease in the later ages. It had been reported that the prevalence of significant obstructive coronary artery disease with stenosis of more than 50% ranged from 27% in women aged less than 50 years up to 64% for women over 80 years old.21

**CONCLUSIONS:** Though the conventional risk factors play an important role in the manifestation of coronary artery disease, presence of significant coronary artery disease in premenopausal women needs further evaluation for non-conventional risk factors.
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| Baseline characteristics | Pre-menopausal (n=125) | Post-menopausal (n=223) |
|--------------------------|------------------------|-------------------------|
| Mean age (±SD)           | 44.29 (±6.44)          | 61.04(±6.17)            |
| Mean SBP (±SD)           | 142.14 (±30.18)        | 138.00(±25.16)          |
| Mean DBP(±SD)            | 85.07 (±11.22)         | 61.04(±6.17)            |
| Diabetes mellitus number (%) | 48 (38.4)       | 127 (57.4)              |

Table 1: Baseline characteristics in pre-menopausal and post-menopausal women

The table shows a higher prevalence of diabetes in postmenopausal subjects than premenopausal subjects. No significant difference was present in systolic blood pressure. Postmenopausal women had lower mean diastolic blood pressure.

Diagram 1: Proportion of pre-menopausal women to Post-menopausal women. Presenting for coronary angiogram

Diagram shows the distribution of postmenopausal and premenopausal subjects undergoing coronary angiography with postmenopausal subjects outnumbering Premenopausal subjects.
Diagram 2: Clinical presentation of coronary artery disease in Pre-menopausal and post-menopausal subjects

Diagram shows higher proportion of subjects presenting with acute coronary events in postmenopausal group and chronic stable angina in premenopausal group.

Diagram 3: Incidence (in percentage) of coronary artery disease in Pre-menopausal and post-menopausal subjects by coronary angiogram

Diagram shows predominance of mild coronary artery disease in premenopausal subjects. Severe coronary artery disease was more frequently seen in post-menopausal subjects.

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