

Comparison of Angiographic Severity of Coronary Artery Disease between Premenopausal and Postmenopausal Women with Acute Coronary Syndrome

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Abstract:

Background: The risk of coronary artery disease in women after menopause sharply rises in contrast to that of women before menopause because of hormonal protection against atherosclerosis. No research work has been done so far to see the angiographic pattern and severity of coronary artery disease in premenopausal women and their comparison with those of postmenopausal women. This study will help understand the pattern and severity of CAD both in premenopausal and postmenopausal women.

Methods: This cross sectional analytical study was conducted over 100 ACS female patients who were purposively selected and agreed to do coronary angiogram during index hospital admission. Among them 50 patients were premenopausal status with CAD constituted study group I and another 50 postmenopausal women with CAD constituted study group II. The main objective of the study was to compare the angiographic severity of coronary artery disease between premenopausal and postmenopausal women with acute coronary syndrome. Angiographic severity of CAD was assessed by vessel score, Gensini score and Friesinger score.

Results: LAD was the common artery involved (76% vs. 56%) followed by RCA (72% vs. 36%) and LCX (62% vs. 30%) in group-II compared to group-I and involvement of individual coronary artery was statistically significant (P values were 0.03, 0.003 and 0.001 respectively). Critical

stenosis (70-99%) involving the all three major epicardial vessels (LAD, LCX and RCA) were found most frequently in group-II and the percentage of lesions were 56% vs. 30%; 56% vs. 22% and 54% vs. 22% respectively ($p < 0.05$). The vessel score of the study patients revealed that single vessel involvement was significantly higher in group-I (52% vs. 24%) ($p=0.003$) and triple vessel involvement was found significantly higher in group-II (40% vs. 12%) ($p=0.001$).

Severity assessment by Friesinger score showed normal (0) and low (1-4) Friesinger score significantly higher in group-I patients ($P=0.04$ and $P=0.007$ respectively) and high Friesinger score (11-15) was found significantly higher in patients in group II ($p=0.001$). Severity assessment by Gensini score of the study patients revealed significantly higher mild Gensini score in group-I patients ($P=0.002$) and severe Gensini score in group II patients ($p=0.002$).

Conclusion: Coronary artery disease is one of the major important problems not only in postmenopausal women but in premenopausal women also. Postmenopausal women suffer from more triple vessels involvement, more diffuse and severe disease. This study results point out that premenopausal women suffer from less severe coronary artery disease and there is a trend to involve mid LAD more frequently in comparison to other two major coronary arteries and LM coronary artery in comparison to postmenopausal women.

Keywords: Acute coronary syndrome (ACS), Angiographic severity, Premenopausal and postmenopausal women.

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Introduction:

Cardiovascular disease (CVD) is the highest single cause of mortality and morbidity in women worldwide.¹ It is the largest single cause of death among women, accounting for one-third of all deaths.² In Bangladesh it is the fourth common cause of death and accounts for 10.68% of total death, of which male 12.47% and female 8.19%.³ In fact, the incidence of Coronary artery disease (CAD) in women older than 65 years is similar to that in men and even surpasses than in men after 75.⁴ The risk of coronary artery disease in women after menopause sharply rises in contrast to that of women before menopause because of hormonal protection against atherosclerosis.⁵

Menopause is a normal biological event that occurs in every woman during their late 40s or early 50s and marked by end of menstrual period. During menopause, women's oestrogen levels become approximately one-third of that during her premenopausal years.⁶ With the changes in the production of female hormones after menopause, the risk of ischemic heart disease and cerebrovascular accident (CVA) are increased which are the main causes of morbidity and mortality in women of both developed and developing countries.⁷ This era of globalization, female education, women empowerment, urbanization and industrialization, has changed the socioeconomic status and lifestyle of women. Modern women have professional and housewife responsibilities, consume excess fat and carbohydrates, smoke, do not exercise regularly and do not have enough time to rest. This situation leads to overweight, dyslipidemia, arterial hypertension, impaired glucose tolerance and diabetes mellitus. As a result increasing number of young women is now suffering from coronary artery disease, not only in western and industrialized countries but also in the Asian countries. Women do not often participate in preventive studies and undergo less intensive and invasive evaluation and treatment of chest pain when compared to men. However, the rate of coronary death is twice higher in women than in men after acute coronary syndromes and revascularization procedures. No research work has been done so far to see the angiographic pattern and severity of coronary artery disease in premenopausal women and their comparison with those of postmenopausal women. So, this study was designed to understand the pattern and severity of CAD both in premenopausal and postmenopausal women and also for risk stratification, and formulation of preventive strategies for these two groups of population.

Materials and methods:

This cross sectional analytical study with group comparison was conducted in the National Institute of

Cardiovascular Diseases (NICVD), Dhaka from January 2013 to July 2014. Both premenopausal and postmenopausal women were purposively selected with ACS and agreed to do coronary angiography (CAG) during index hospital admission. Total 100 patients were included in the study and divided into two groups according to their menstrual history. Group I comprises 50 premenopausal women and Group II comprises 50 postmenopausal women. Both premenopausal and postmenopausal women with previous history of PCI, CABG, valvular heart disease, cardiomyopathy, hysterectomy and oophorectomy were excluded from the study. The study protocol was approved by Ethical Review Committee of NICVD. Informed consent was taken from each patient.

Assessment of angiographic pattern and severity of CAD:

Coronary angiography was done during same hospital stay. Interpretation of coronary angiogram was done by visual estimation by two cardiologists to assess the severity of CAD. Severity of coronary stenosis was graded according to the number of major epicardial vessel with significant stenosis (vessel score), Gensini score and Friesinger score.

A. Vessel score:⁸

This is the number of vessels with a significant stenosis (for left main coronary artery 50% or greater and for others 70% or greater reduction in luminal diameter). Score ranged from 0 to 3, depending on the number of vessel involved.

- Score 0 = no vessel involvement.
- Score 1 = single vessel involvement.
- Score 2 = double vessel involvement.
- Score 3 = triple vessel involvement.

B. Gensini score:⁹

The Gensini score was developed by Gensini taking into consideration the geometrical severity of lesion by angiography, the cumulative effects of multiple obstructions, and the significance of jeopardized myocardium.

Table-I

Shows CAD severity according to Gensini scores

| Scores | CAD severity |
|-------------|--------------------|
| ≤36 points | Mild or absent |
| > 36 points | Moderate to severe |

Quantitative analysis was performed by using the Gensini score.

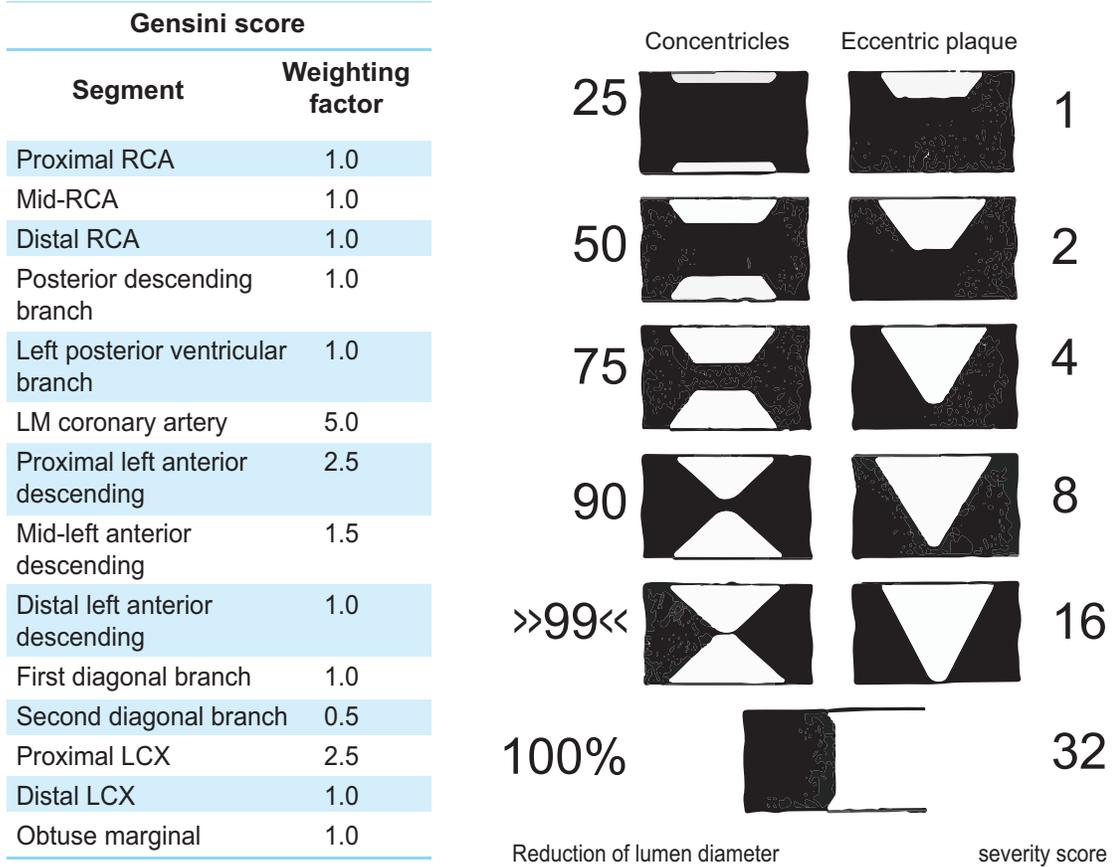


Fig.-1: Gensini Score chart [Left panel- weighting factor according to the importance of vessel in the coronary tree.¹⁰ Right panel-severity score according to reduction of lumen diameter.¹¹

C. Friesinger score:⁸

The Friesinger index is a score ranges from 0 to 15. Each of the three main coronary arteries was scored separately from 0 to 5.

- Score 0 : No arteriographic abnormality
- Score 1 : Trivial irregularities (lesion from 1-29%)
- Score 2 : Localized 30-68% luminal narrowing
- Score 3 : Multiple 30-68% luminal narrowing of same vessel
- Score 4 : 69-100% luminal narrowing without 100% occlusion of proximal segments
- Score 5 : Total obstruction of a proximal segment of a vessel.

Statistical Methods:

The numerical data obtained from the study were analyzed and significance of differences was estimated by using statistical methods. The SPSS Statistical Software (17.0 version, SPSS Inc., Chicago, Illinois, USA) was used for data analysis. Continuous variables were

expressed as mean and standard deviation and categorical variables as frequency and percentage. Student's t-test was used to compare normally distributed continuous variables and for the categorical variables the chi-square test was done. To identify independent effects risk factors on CAD severity multiple logistic regression analysis was done. P value of less than 0.05 was considered as significant.

Results:

This study was done to compare the angiographic severity of coronary artery disease between premenopausal and postmenopausal women with acute coronary syndrome. A total of 100 ACS female patients undergoing coronary angiography were studied. Among them 50 patients were premenopausal status with CAD constituted study group I and another 50 postmenopausal women with CAD constituted study group II.

Among the studied patients, highest percentage had history of hypertension (76%) followed by diabetes

mellitus (68%), family history of premature CAD (58%), past OCP user(58%), chewing tobacco (50%) and dyslipidaemia (36%) in group II. Chewing tobacco, hypertension past OCP user and diabetes mellitus were observed significantly ($p<0.05$) higher among the group II patients than those of the group I patients. On the

contrary, OCP user (76%), hypertension (54%), diabetes mellitus (46%), and family history of CAD (42%) were the most common risk factors in group I patients. OCP users were found significantly ($p=0.001$) higher in group I patients than those of group II patients.

Table-II
Distribution of the patients according to risk factors

| Risk Factors | Group I (n= 50) | | Group II (n=50) | | Total (n=100) | | p value |
|-------------------|-----------------|------|-----------------|------|---------------|------|--------------------|
| | Number | % | Number | % | Number | % | |
| Smoking | | | | | | | |
| Yes | 10 | 20.0 | 7 | 14.0 | 17 | 17.0 | 0.42 ^{NS} |
| No | 40 | 80.0 | 43 | 86.0 | 83 | 83.0 | |
| Chewing tobacco | | | | | | | |
| Yes | 6 | 12.0 | 25 | 50.0 | 31 | 31.0 | 0.001 ^S |
| No | 44 | 88.0 | 25 | 50.5 | 69 | 69.0 | |
| Hypertension | | | | | | | |
| Yes | 27 | 54.0 | 38 | 76.0 | 65 | 65.0 | 0.02 ^S |
| No | 23 | 46.0 | 12 | 24.0 | 35 | 35.0 | |
| Dyslipidaemia | | | | | | | |
| Yes | 10 | 20.0 | 18 | 36.0 | 28 | 28.0 | 0.07 ^{NS} |
| No | 40 | 80.0 | 32 | 64.0 | 72 | 72.0 | |
| Family H/O of CAD | | | | | | | |
| Yes | 21 | 42.0 | 29 | 58.0 | 50 | 50.0 | 0.11 ^{NS} |
| No | 29 | 58.0 | 21 | 42.0 | 50 | 50.0 | |
| Diabetes mellitus | | | | | | | |
| Yes | 23 | 46.0 | 34 | 68.0 | 57 | 57.0 | 0.02 ^S |
| No | 27 | 54.0 | 16 | 32.0 | 43 | 43.0 | |
| OCP use | | | | | | | |
| Never | 12 | 24.0 | 20 | 40.0 | 32 | 32.0 | 0.08 ^{NS} |
| Current user | 25 | 50.0 | 1 | 2.0 | 26 | 26.0 | 0.001 ^S |
| Past user | 13 | 26.0 | 29 | 58.0 | 42 | 42.0 | 0.001 ^S |

Group I: Premenopausal women
NS= Not significant ($p>0.05$)
P value reached from Chi Square test.

Group II: Postmenopausal women
S = Significant ($p<0.05$)

Table-III
Distribution of study population by involvement of individual coronary artery (n=100)

| Artery | Group I (n= 50) | | Group II (n =50) | | p value |
|---------|-----------------|------|------------------|------|--------------------|
| | Number | 1% | Number | % | |
| LM | | | | | |
| Present | 8 | 16.0 | 3 | 6.0 | 0.11 ^{NS} |
| Absent | 42 | 84.0 | 47 | 94.0 | |
| LAD | | | | | |
| Present | 28 | 56.0 | 38 | 76.0 | 0.03 ^S |
| Absent | 22 | 44.0 | 12 | 24.0 | |
| LCX | | | | | |
| Present | 15 | 30.0 | 31 | 62.0 | 0.001 ^S |
| Absent | 35 | 70.0 | 19 | 38.0 | |
| RCA | | | | | |
| Present | 18 | 36.0 | 36 | 72.0 | 0.003 ^S |
| Absent | 32 | 64.0 | 14 | 28.0 | |

Group I: Premenopausal women
NS= Not significant ($p>0.05$)
p value reached from Chi Square test.

Group II: Postmenopausal women
S = Significant ($p<0.05$)

The table shows distribution of involvement of individual major coronary artery among the study population. Involvement of three coronary arteries including LAD, LCX and RCA was found significantly higher percentage in group-II patients compared to group-I patients (76% vs. 56%; 62% vs. 30% and 72% vs. 36% respectively). Interestingly LM involvement was found higher in number in group-I patients (16% vs. 6%) but it was statistically insignificant (P=0.11)

Normal LAD vessel was found 22 (44%) patients in group I and 12 (24%) patients in group II. Proximal LAD lesion was found 9 (18%) and 20 (40%) in group I and group II respectively. Mid LAD lesion was found 16 (32%) and 17 (34%) in group I and group II respectively. Distal lesion was found 3 (6%) in group I and 1 (2%) in group II. Analysis revealed that normal LAD vessel was significantly higher in group I (p=0.03) and proximal LAD lesion was significantly higher in group II (p=0.01).

Regarding the site of lesion of LCX, normal vessel was found 35 (70%) patients in group I and 19 (38%) patients in group II. Proximal lesion was found 3 (6%) and 14 (28%) in group I and group II respectively. Mid lesion was

found 1 (2%) and 4 (8%) in group I and group II respectively. Distal lesion was found 11 (22%) in group I and 13 (26%) in group II. Analysis revealed that normal LCX vessel was significantly higher in group I (p=0.001) and proximal lesion in LCX was significantly higher in group II (p=0.003).

RCA normal vessel was found 32 (64%) patients in group I and 14 (28%) patients in group II. Proximal segment involvement was found 8 (16%) and 15 (30%) in group I and group II respectively. Mid lesion was found 7 (14%) and 14 (28%) in group I and group II respectively. Distal lesion was found 3 (6%) in group I and 7 (14%) in group II. Analysis revealed that normal RCA vessel was significantly higher in group I (p=0.001).

Regarding the site of coronary artery lesion normal LM was found in 42 (84%) and 47 (94%) patients in group I and group II respectively. Diseased LM was involved 8 (16%) in group I and 3 (6%) in group II respectively. Normal LM was not significantly higher in group II (p=0.11) and diseased LM was also not significantly higher in group I (p=0.11).

Table IV
Distribution of study patients by site of coronary artery lesion

| Site of lesion | Group I (n= 50) | | Group II (n =50) | | p value |
|-----------------|-----------------|------|------------------|------|--------------------|
| | Number | % | Number | % | |
| LAD | | | | | |
| Normal | 22 | 44.0 | 12 | 24.0 | 0.03 ^S |
| Proximal lesion | 9 | 18.0 | 20 | 40.0 | 0.01 ^S |
| Mid lesion | 16 | 32.0 | 17 | 34.0 | 0.83 ^{NS} |
| Distal lesion | 3 | 6.0 | 1 | 2.0 | 0.30 ^{NS} |
| LCX | | | | | |
| Normal | 35 | 70.0 | 19 | 38.0 | 0.001 ^S |
| Proximal lesion | 3 | 6.0 | 14 | 28.0 | 0.003 ^S |
| Mid lesion | 1 | 2.0 | 4 | 8.0 | 0.18 ^{NS} |
| Distal lesion | 11 | 22.0 | 13 | 26.0 | 0.63 ^{NS} |
| RCA | | | | | |
| Normal | 32 | 64.0 | 14 | 28.0 | 0.001 ^S |
| Proximal lesion | 8 | 16.0 | 15 | 30.0 | 0.09 ^{NS} |
| Mid lesion | 7 | 14.0 | 14 | 28.0 | 0.08 ^{NS} |
| Distal lesion | 3 | 6.0 | 7 | 14.0 | 0.18 ^{NS} |
| LM | | | | | |
| Normal | 42 | 84.0 | 47 | 94.0 | 0.11 ^{NS} |
| Diseased | 8 | 16.0 | 3 | 6.0 | 0.11 ^{NS} |

Group I: Premenopausal women

Group II: Postmenopausal women

NS= Not significant (p>0.05)

S = Significant (p<0.05)

p value reached from Chi Square test and Fisher's exact test.

Table-V
Distribution of study patients by percentage of coronary artery lesion

| Percentage of lesion | Group I (n= 50) | | Group II (n =50) | | p value |
|----------------------|-----------------|------|------------------|------|--------------------|
| | Number | % | Number | % | |
| LAD | | | | | |
| <70% | 6 | 12.0 | 4 | 8.0 | 0.50 ^{NS} |
| 70-99% | 15 | 30.0 | 28 | 56.0 | 0.008 ^S |
| 100% | 7 | 14.0 | 6 | 12.0 | 0.76 ^{NS} |
| LCX | | | | | |
| <70% | 2 | 4.0 | 3 | 6.0 | 0.64 ^{NS} |
| 70-99% | 11 | 22.0 | 28 | 56.0 | 0.001 ^S |
| 100% | 2 | 4.0 | 0 | 0.0 | 0.25 ^{NS} |
| RCA | | | | | |
| <70% | 2 | 4.0 | 3 | 6.0 | 0.64 ^{NS} |
| 70-99% | 11 | 22.0 | 27 | 54.0 | 0.001 ^S |
| 100% | 5 | 10.0 | 6 | 12.0 | 0.75 ^{NS} |

Group I: Premenopausal women

Group II: Postmenopausal women

NS= Not significant (p>0.05)

S = Significant (p<0.05)

p value reached from Chi Square test and Fisher's exact test.

Regarding the percentage of lesion in LAD, <70% lesions were found 6 (12%) patients in group I and 4 (8%) patients in group II. 70-99% lesions were found 15 (30%) patients in group I and 28 (56%) in group II. 100% lesion was found 7 (14%) patients in group I and 6 (12%) patients in group II. Observation revealed that 70-90% lesions was significantly higher in group II than group I (p=0.008).

Regarding the percentage of lesion in LCX, <70% lesions were found 2 (4%) patients in group I and 3 (6%) patients in group II. 70-99% lesions were found 11 (22%) patients in group I and 28 (56%) in group II. 100% lesion was found 2 (4%) patients in group I but no patients in group II. Observation revealed that 70-90% lesions was significantly higher in group II than group I (p=0.001).

Regarding the percentage of lesion in RCA, <70% lesions were found 2 (4%) patients in group I and 3 (6%) patients in group II. 70-99% lesions were found 11 (22%) patients in group I and 27 (54%) in group II. 100% lesion was found 5 (10%) patients in group I and 6 (12%) patients in group II. Observation revealed that 70-90% lesions was significantly higher in group II than group I (p=0.001).

In LCX, type-A lesion was found 10 (20%) patients in group I and 7 (14%) patients in group II. Type B lesion was found in 3 (6%) patients in group I and 15 (30%) patients in group II. Type C lesion was found in 2 (4%) patients in group I and 9 (18%) patients in group II. It was observed that type B lesion was significantly higher in group II than group I (p=0.001). It was also observed that

type C lesion was significantly higher in group II than group I (p=0.03).

In RCA, type A lesion was found in 12 (24%) patients in group I and 18 (36%) patients in group II. Type B lesion was found in 5 (10%) patients in group I and 14 (28%) patients in group II. Type C lesion was found in 1 (2%) patients in group I and 4 (8%) patients in group II. It was observed that type B lesion was significantly higher in group II than group I (p=0.02).

The below table shows the vessel score of the study patients. It was found that among group I patients, highest percentage had single vessel score 52% followed by double vessel score 24% and 12% patient had triple vessel score and no vessel score. On the contrary among group II patients, highest percentage had triple vessel score 40% followed by double, single and no vessel score 34% & 24% and 2% patients respectively. No vessel involvement was found insignificant in both groups (p=0.05). The table depicted that single vessel involvement was observed significantly higher in group I than group II (p=0.003). On the other hand, triple vessel involvement was found significantly higher in group II than group I (p=0.001)

The below table shows that normal Friesinger score (0) was found in 6 (12%) patients in group I and 1 (2%) patients in group II. Low Friesinger score (1-4) was found in 20 (40%) and 8 (16%) patients in group I and group II respectively. Hence, normal and low Friesinger score were higher and statistically significant in group I (p=0.04)

and $p=0.007$ respectively). Intermediate Friesinger score (5-10) was found in 21 (42%) patients in group I and in 25 (50%) patients in group II. Intermediate Friesinger Score was found higher in group II but it was not statistically significant ($p=0.42$). High Friesinger score (11-15) was found in 3 (6%) patients in group I and 16 (32%) patients in group II. High Friesinger score was significantly higher in group II ($p=0.001$).

Below table shows Gensini score of the study patients. Mild Gensini score was 38 (76%) patients in group I and 23 (46%) patients in group II. Severe Gensini score was found 12 (24%) patients in group I and 27 (54%) patients in group II. The table observed that severe Gensini score was significantly higher in group II patients than group I ($p=0.002$) and mild Gensini score was significantly higher in group I patients than group II ($p=0.002$).

Table IX demonstrates the binary logistic regression analysis of Odds Ratios for characteristics of the patients likely to be associated with coronary artery disease severity among postmenopausal women. Results of binary logistic regression analysis for severe CAD showed that age, chewing tobacco, hypertension and diabetes mellitus were significantly related to the degree of severity of CAD ($p<0.05$). The above table also revealed

that among postmenopausal women age ≥ 50 , chewing tobacco, hypertension and diabetes mellitus of CAD with ORs being 2.836, 1.625, 1.235 and 1.837 in univariate analysis respectively. It was also observed that among postmenopausal patients age ≥ 50 , chewing tobacco, hypertension and diabetes mellitus of CAD with ORs being 2.426, 1.490, 1.219 and 1.670 in multivariate analysis respectively.

The below table demonstrates the binary logistic regression analysis of Odds Ratios for characteristics of the patients likely to be associated with coronary artery disease severity among premenopausal women. Results of binary logistic regression analysis for severe CAD were shown for chewing tobacco, hypertension, diabetes mellitus, and family history of CAD and OCP users to the degree of severity of CAD. The above table revealed that among premenopausal women who used OCP have 1.932 times the risk of having significant ($p=0.01$) CAD as those who never used OCP in univariate analysis. The above table also revealed that among premenopausal women who used OCP have 1.792 times the risk of having significant ($p=0.02$) CAD as those who never used OCP in multivariate analysis. So, OCP use in premenopausal women has a significant association with the severity of CAD.

Table-VI
Distribution of the study patients according to vessel score

| Vessel Score | Group I (n= 50) | | Group II (n =50) | | p value |
|--------------|-----------------|------|------------------|------|--------------------|
| | Number | % | Number | % | |
| Score – 0 | 6 | 12.0 | 1 | 2.0 | 0.05 ^{NS} |
| Score – 1 | 26 | 52.0 | 12 | 24.0 | 0.003 ^S |
| Score – 2 | 12 | 24.0 | 17 | 34.0 | 0.27 ^{NS} |
| Score – 3 | 6 | 12.0 | 20 | 40.0 | 0.001 ^S |

Group I: Premenopausal women

Group II: Postmenopausal women

NS= Not significant ($p>0.05$)

S = Significant ($p<0.05$)

p value reached from Chi Square test and Fisher's exact test.

Table-VII
Distribution of the study patients according to Friesinger score

| Friesinger Score | Group I (n= 50) | | Group II (n =50) | | p value |
|-----------------------|-----------------|------|------------------|------|--------------------|
| | Number | % | Number | % | |
| Normal (0) | 6 | 12.0 | 1 | 2.0 | 0.04 ^S |
| Low (1 – 4) | 20 | 40.0 | 8 | 16.0 | 0.007 ^S |
| Intermediate (5 – 10) | 21 | 42.0 | 25 | 50.0 | 0.42 ^{NS} |
| High (11 – 15) | 3 | 6.0 | 16 | 32.0 | 0.001 ^S |

Group I: Premenopausal women

Group II: Postmenopausal women

NS= Not significant ($p>0.05$)

S = Significant ($p<0.05$)

p value reached from Chi Square test and Fisher's exact test.

Table-VIII
Distribution of the study patients according to Gensini score

| Gensini Score | Group I (n= 50) | | Group II (n =50) | | p value |
|------------------|-----------------|------|------------------|------|--------------------|
| | Number | % | Number | % | |
| Severe CAD (>36) | 12 | 24.0 | 27 | 54.0 | 0.002 ^S |
| Mild CAD (≤36) | 38 | 76.0 | 23 | 46.0 | 0.002 ^S |

Group I: Premenopausal women Group II: Postmenopausal women
NS= Not significant (p>0.05) S = Significant (p<0.05)
p value reached from Chi Square test.

Table-IX
Predictors of severe coronary artery disease (Gensini score >36) with risk factors among postmenopausal women (n=50)

| Variables of interest | Univariate analysis | | Multivariate analysis | |
|-----------------------|---------------------|--------------------|-----------------------|--------------------|
| | OR (95% CI) | P value | OR (95% CI) | P value |
| Age ≥50 | 2.836 (1.237-6.506) | 0.01 ^S | 2.426 (1.127-5.206) | 0.02 ^S |
| Chewing tobacco | 1.625 (1.320-4.984) | 0.02 ^S | 1.490 (1.304-4.294) | 0.03 ^S |
| Hypertension | 1.235 (1.220-4.532) | 0.03 ^S | 1.219 (1.119-3.491) | 0.04 ^S |
| Dyslipidemia | 1.015 (0.372-2.077) | 0.16 ^{NS} | 0.992 (0.472-1.912) | 0.20 ^{NS} |
| Diabetes mellitus | 1.837 (1.234-6.103) | 0.03 ^S | 1.670 (1.291-5.32) | 0.02 ^S |
| Family history of CAD | 0.919 (0.411-2.054) | 0.25 ^{NS} | 0.822 (0.391-2.001) | 0.29 ^{NS} |

S=Significant
Ns=Not significant

Table-X
Predictors of severe coronary artery disease (Gensini score >36) with risk factors among premenopausal women (n=50)

| Variables of interest | Univariate analysis | | Multivariate analysis | |
|-----------------------|---------------------|--------------------|-----------------------|--------------------|
| | OR (95% CI) | P value | OR (95% CI) | P value |
| Chewing tobacco | 0.640 (0.099-5.789) | 0.59 ^{NS} | 0.500 (0.045-5.612) | 0.54 ^{NS} |
| Hypertension | 1.401 (0.345-6.290) | 0.61 ^{NS} | 1.392 (0.313-6.196) | 0.66 ^{NS} |
| Diabetes mellitus | 1.202 (0.289-4.823) | 0.79 ^{NS} | 1.162 (0.281-4.810) | 0.83 ^{NS} |
| Family history of CAD | 0.439 (0.096-1.910) | 0.17 ^{NS} | 0.386 (0.086-1.713) | 0.21 ^{NS} |
| OCP user | 1.932 (1.029-3.840) | 0.01 ^S | 1.792 (1.021-3.810) | 0.02 ^S |

S=Significant
NS=Not significant

Discussion:

This cross sectional observational study was conducted in National Institute of Cardiovascular Diseases (NICVD), Dhaka, from January 2013 to June 2014. The main objective of the study was to compare the severity of coronary artery disease between premenopausal and postmenopausal women with acute coronary syndromes. A total of 100 patients with acute coronary syndromes enrolled on the basis of predefined inclusion and exclusion criteria who underwent coronary

angiography were included in the study. Based on menopausal status, the patients were divided into two groups. 50 patients were premenopausal status with ACS and constituted study group I and the other 50 patients were postmenopausal status with ACS who constituted group II.

The age distribution of most of the patients in group I belonged to 41-50 years of age, which were 30 (60%) and in group II belonged to 51 to 60 years of age and were 21 (42%). The mean age of the studied patients

was a 48.8 ± 9.2 year ranging from 32 to 75 years. The mean age of the group I patients was 41.6 ± 3.8 years ranging from 32 to 46 years and the mean age of the group II patients was 56.0 ± 7.2 years ranging from 48 to 75 years. The mean age difference of the two groups were observed statistically significant ($p < 0.05$). This age distribution corresponds with the age distribution of population of related study done by Majumder, et al. where mean age of postmenopausal women was (56.8 ± 6.5) years.¹²

Regarding the risk factors among the studied patients, it was observed that hypertension (76%) followed by diabetes mellitus (68%), family history of CAD (58%), past OCP user (58%), chewing tobacco (50%) and dyslipidaemia (36%) were the most common risk factors in postmenopausal women and on the other hand, OCP user (76%), hypertension (54%), diabetes mellitus (46%) and family history of coronary artery disease (42%) were the most common risk factors in premenopausal women. Chewing tobacco, hypertension and diabetes mellitus were observed significantly ($p < 0.05$) higher among the postmenopausal women than those of the premenopausal women. In a study by Shehab, et al. in postmenopausal women found that hypertension, diabetes mellitus and dyslipidemia were the major risk factors for CAD (65.7%, 52.9% and 42.2% respectively).¹³ In a similar study by Ke-fei, et al. hypertension, (55.0% vs.66.0%), Diabetes mellitus,(15.0% vs.31.5%) and Dyslipidemia, (23.9% vs.37.4%) were the most common major risk factors among premenopausal and postmenopausal women.¹⁴ The prevalence of hypertension, diabetes mellitus and dyslipidemia in these studies exactly correlate with those of the present study.

Angiographic findings of both premenopausal and postmenopausal women showed normal CAG in 12% of premenopausal and 2% of postmenopausal women. Regarding the lesion characteristics, type-B and type-C lesion were found significantly high in postmenopausal women. Type-B lesions was found statistically significant different in LCX ($P = 0.001$) and RCA ($P = 0.02$) and type-C lesion in LAD ($P = 0.04$) and LCX (0.03) respectively in two groups.

Distribution of involved coronary arteries in group-I revealed involvement of LM artery was 16%, LAD artery was 56%, LCX artery was 30% and RCA was 36%, and in group-II involvement of LM artery was 6%, LAD was 78%, LCX was 62% and RCA was 72%. LAD was the common artery involved (76% vs.56%) followed by RCA (72% vs. 36%) and LCX (62% vs. 30%) in group-II

compared to group-I. This frequency of involvement of individual coronary artery in group-II was statistically significant (P values were 0.03, 0.003 and 0.001 respectively).

In a study, Akanda, et al. found that LAD was the most frequently involved artery (88.0%), followed by RCA (78.07%), LCX (52.61%) and LM (5.26%) in descending order of frequency.¹⁵ This order of involvement of coronary arteries exactly correlated with that of our study. In group-I more frequently involved vessel was LAD (56%) followed by RCA (36%) and LCX (30%). In studies with premenopausal women by ke-fei, et al.¹⁴ Nagamalesh, et al.¹⁶ and Xie, et al.¹⁷ LAD was found common culprit vessel which was 77.1%, 64.51% and 71.8% respectively. This frequency of LAD involvement in premenopausal women also correlates with findings of this study as LAD (56%) was the most common diseased vessel in premenopausal women.

Regarding the percentage of lesion, critical stenoses (70-99%) involving the all three major epicardial vessels (LAD, LCX and RCA) were found most frequently in group-II in respect to group-I and the percentage of lesions were 56% vs. 30%; 56% vs. 22% and 54% vs. 22% respectively. This observation was statistically significant ($p < 0.05$) between two groups.

Proximal segment involvement in all three coronary arteries was found higher frequency in group-II and percentage of involvement was in LAD, 40% vs. 18%; LCX, 28% vs. 6% and RCA, 30% vs. 16% respectively. There was statistically significant difference in the involvement of proximal LAD and LCX between two groups ($P < 0.05$), Proximal and mid LAD lesions were a frequent finding in group-I (18% and 32%). Ke-fei, et al.¹⁴ revealed that proximal LAD also a frequently involved vessel in both premenopausal and postmenopausal women (50.4% vs.38.0%) but involvement of proximal LCX and RCA was higher in postmenopausal women (47% vs. 33.9% and 21.6% vs. 19.3%). LM disease was 9.6% vs.10.8%.These findings were almost similar to the findings of our study.

The vessel score of the study patients showed highest percentage of single vessel involvement in group-I (52% vs.34%) and triple vessel involvement in group-II patients (40% vs. 12%). This observation revealed that single vessel involvement was significantly higher in group-I than group-II ($p = 0.003$). On the other hand, triple vessel involvement was found significantly higher in group-II than group-I ($p = 0.001$). The vessel score of this study was similar to the score in the study done by Ke-fei, et al.¹⁴ where single vessel score in premenopausal

women was, 43.2% vs. 26.9% and triple vessel score in postmenopausal women was, 33.8% vs. 20.4%. Nagamalesh, et al.¹⁶ and Xie, et al.¹⁷ in their studies with premenopausal women found single vessel involvement most frequently (87.05% and 71.8% respectively).

Severity assessment by Friesinger score showed normal (0) and low (1-4) Friesinger score higher in group-I patients (12% vs.2% and 40% vs. 16% respectively) and statistically significant ($P=0.04$ and $P=0.007$ respectively). High Friesinger score (11-15) was found higher in patients in group II (32%vs. 32%). High Friesinger score was also significantly higher in group II ($p=0.001$).

Severity assessment by Gensini score of the study patients revealed mild Gensini score in group-I patients (76% vs. 46%) and significantly higher in compared to group-II patients ($P=0.002$). On the other hand, severe Gensini score was found in group-II patients (54% vs. 24%) and this severe Gensini score was significantly higher in group II patients than group I ($p=0.002$).

The binary logistic regression analysis for severe CAD among postmenopausal women showed that age, chewing tobacco, hypertension and diabetes mellitus were significantly related to the degree of severity of CAD ($p<0.05$) with ORs being 2.836, 1.625, 1.235 and 1.837 respectively in 'univariate analysis and 2.426, 1.490, 1.219 and 1.670 respectively in multivariate analysis.

The binary logistic regression analysis for severe coronary artery disease with the risk factors among the premenopausal women revealed that OCP users have 1.932 times the risk of having significant ($p=0.01$) CAD in compared to those who never used OCP in univariate analysis and 1.792 times the risk of having significant ($p=0.02$) CAD as those who never used OCP in multivariate analysis. So, OCP use in premenopausal women has a significant association with the severity of CAD.

The logistic regression analysis revealed that not only the withdrawal of protective effect of estrogens in postmenopausal women contribute to put them at increased risk of having acute coronary syndrome but several other risk factors including age, chewing tobacco and diabetes mellitus found in this study were also strongly related to the severity of CAD and on the other hand OCP significantly influenced the severity CAD among the premenopausal women.

Conclusion:

Coronary artery disease is one of the major important problems not only in postmenopausal women but in

premenopausal population also. Postmenopausal women suffer from more triple vessels involvement, more diffuse and severe disease. This study results point out that premenopausal women suffer from less severe coronary artery disease and there is a trend to involve mid LAD more frequently in compared to other two major coronary arteries and LM coronary artery in compared to their counterpart, postmenopausal women.

Study limitation:

There was selection bias as assignment of patients to either group was not randomized. Only hospitalized patients were studied here so may not be applicable to the general population. Menopausal status was determined on the basis of menstrual history rather than on the basis of hormonal changes. Angiographic severity of coronary artery disease was evaluated by visual estimation, so chance of interobserver and intraobserver variation is likely to be present.

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