

**A STUDY OF CLINICO -EPIDEMIOLOGICAL AND CORONARY
ANGIOGRAPHICAL PROFILE OF PRE MENOPAUSAL WOMEN WITH ACUTE
CORONARY SYNDROME IN A TERTIARY CARE HOSPITAL**

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ABSTRACT

Background: Even though Coronary artery disease is one of the leading cause of death globally for both male and female, there is limited data on acute coronary syndrome among pre-menopausal women .The management of acute coronary syndrome is based on rapid diagnosis in order to provide treatment. Female gender is strongly correlated with delayed hospital arrival due to due to low awareness, sociocultural and financial reasons. Risk factors, pathophysiology, presentation may vary in female compared to male. For many years, women have been underdiagnosed and undertreated.

Objective: In our study objective was to assess the additional risk factors in pre-menopausal women for Acute Coronary Syndrome and to evaluate the biochemical, electrocardiogram, echocardiography profile and coronary angiographic profile.

Methods: This was cross-sectional observational study conducted in Cardiology department of a tertiary care Hospital, West Bengal over a period of 1 yr. The study was conducted over 100 pre-menopausal women patients admitted with Acute Coronary Syndrome in cardiology ward and intensive coronary care unit after fulfilling inclusion and exclusion criteria. All study patients underwent complete physical, biochemical and relevant investigation including Electrocardiogram, Echocardiogram followed by coronary angiography. All data were collected and analysed statistically.

Results: This study had shown that young women presenting with ACS (Acute Coronary Syndrome) had significant comorbidities. The mean ($\pm$ SD) age of the study population was

41.10 (± 5.002) years. On echocardiography 49% of study patients had Anterior wall MI (Myocardial infarction), 29% had inferior wall MI, 7% of subjects had global hypokinesia & 10% had no RWMA (Regional wall motion abnormality). In our study the proportions of subjects with significant LMCA (Left Main Coronary Artery) stenosis, LAD (left anterior descending artery) stenosis, LCX (left circumflex artery) stenosis and RCA (Right coronary artery) stenosis on coronary angiography were 11%, 61%, 28% and 34% respectively. Background variables e.g., age, BMI (body mass index), hypertension, diabetes, dyslipidemia, Family history of AMI (Acute myocardial infarction), NYHA class at presentation and ANA profile of the study subjects were not significantly associated with LMCA stenosis.

Conclusion: AMI incidence is rising in young female in India. The present descriptive observational study was conducted over one year duration among randomly selected 100 pre-menopausal women with Acute Coronary Syndrome. Anterior Wall MI was the most common presentation in our study. Obesity, hypertension, diabetes, dyslipidemia were important risk factors & 5% of the subjects had positive ANA profile in this study.

Keywords- Acute Coronary Syndrome, pre-menopausal women, coronary angiography.

Introduction

Ischemic heart disease causes more deaths and disability and incurs greater economic cost than any other illness in the developed world. Genetic factors, a high fat and energy rich diet, smoking and sedentary lifestyle are associated with the emergence of IHD (Ischaemic heart disease).¹

It encompasses a wide clinical spectrum ranging from silent ischemia to sudden death.²

Patients with IHD fall into two large groups: those who presents with chronic stable angina and patients with acute coronary syndromes (ACS). These include patients with Acute Myocardial Infarction with ST segment elevation (STEMI) on their presenting ECG and those with non-ST elevation ACS. The later includes patient with non-ST segment elevation myocardial infarction (NSTEMI), which, by definition has evidence of myocyte necrosis, and those with unstable angina (UA).³

Within this spectrum, acute ST-segment elevation myocardial infarction (STEMI) is the most significant form of the disease because STEMI represents the most lethal form of ACS and its incidence and case fatality rate is decreasing due to improved management.^{4,5}

The 12 lead ECG is a pivotal diagnostic and triage tool because it is at the centre of the decision pathway and management; it permits distinction of those with STEMI from those having NSTEMI. Serum cardiac biomarkers are used to differentiate UA from NSTEMI.

Coronary artery disease is the leading cause of death globally of all income groups, accounting more than 9 million deaths in 2016. ⁶ Acute myocardial infarction (AMI) has historically been regarded as a man's disease, and for many years, women have been underdiagnosed and undertreated. Bernadine Healy, the erstwhile director of the US National Institutes of Health, classically referred to this as the Yentl syndrome, describing women who were not recognized as experiencing AMI unless they presented with male-pattern chest pain symptoms.⁷ Towfighi et al noted that MI hospitalization rates decreased over time by 26% in men but only 18% in women between the ages of 35 and 64 years.⁸ In fact, MI hospitalization rates increased for women 35–44 years and decreased only slightly for women 45–54 years and men 35–44 years. Approximately 3% to 10% of acute coronary syndrome occurs in young patients (aged <45 years); however, this risk is often underappreciated.⁹

South Asians have increased risk of IHD (ischemic heart disease) compared to other ethnic groups.¹⁰

Female gender is strongly correlated with delayed hospital arrival and symptom to balloon time in STEMI due to low awareness, sociocultural and financial reasons.¹¹

Women of younger age have traditional risk factors of coronary artery diseases like smoking, obesity, diabetes, and hypercholesterolemia.

Non-traditional risk factors like chronic obstructive lung disease, and poor baseline mental health, connective tissue disorders like SLE (Systemic lupus erythematosus), MCTD (Mixed connective tissue disease), Rheumatoid Arthritis with higher inflammatory markers than men.¹³ Certain percentage of young women present with atypical right-sided chest pain, neck or shoulder pain compared with men who experience typical left-sided chest pain radiating to the left shoulder and jaw.¹²

Women tend to have less adverse anatomical characteristics than men with lower plaque burden and less calcification, particularly among younger women.¹³

In our study our aim was to assess the additional risk factors in pre-menopausal women for Acute Coronary Syndrome and to evaluate the biochemical, electrocardiogram, echocardiography profile and coronary angiographic profile.

Materials and methods

This cross-sectional observational study was conducted in Cardiology department of a tertiary care Hospital, West Bengal, India. Over a period of 1 yr, 100 patients admitted with Acute Coronary Syndrome in cardiology ward and intensive coronary care unit were included in our study after fulfilling inclusion and exclusion criteria. This study was conducted over premenopausal women admitted with acute coronary syndrome. Patients with hemodynamically significant valvular heart disease, congenital heart disease, cardiomyopathy, renal failure and who were unwilling to give consent were excluded.

Institutional ethical committee approval was taken. After taking informed consent from each patient detailed history of symptoms and baseline characteristics including clinical parameters, risk factors, demographic data were collected. All study patients underwent complete physical, biochemical and relevant investigation including Electrocardiogram, Echocardiogram followed by coronary angiography. Coronary angiography was performed on all patients in catheterization laboratory (Siemens Artis interventional angiography systems).

The Coronary angiographic study will include measurement of diameter and stenosis severity, qualitative assessment of flow will be documented. Luminal stenosis will be calculated as the percentage of diameter reduction in diseased segment compared to the proximal disease-free reference segment. More than 70% stenosis in either one of three major coronary arteries including the left anterior descending artery (LAD), left circumflex artery (LCX), and right coronary artery (RCA) or their first-order branches and more than 50% stenosis in Left Main Coronary Artery (LMCA) will be considered as significant for CAD.

Collected data were analysed in an excel spread sheet and analysed subsequently using SPSS 24.

Categorical variables were expressed in frequencies and percentages (%). Continuous variables were expressed in mean +SD (standard deviation) or median (inter-quartile range).

Results and analysis

Our study was conducted over one year duration among 100 pre-menopausal women with Acute Coronary Syndrome admitted in cardiology ward and intensive coronary care unit of a tertiary care Hospital, Kolkata. The mean ($\pm$ SD) age of the study population was 41.10 ($\pm$ 5.002) years. 17% of the women were in the age group of 30-35 years, 32% were in between 36-40 years, 28% in 41-45 years and 23% in 45-50 years of age group. According to BMI 30% of the subjects were overweight and 29% were obese. 59% of the women were hypertensive & 47% of the subjects were diabetic. 46% of the subjects were having Dyslipidemia. 25% of the subjects had positive family history of AMI. 31% of the subjects belonged to class 2 of NYHA at presentation. The mean (SD) and median (IQR) systolic blood pressure (SBP) was 122.12 (19.28) mmHg and 120 (104.25, 130) mmHg; and the diastolic blood pressure (DBP) was 79.72 (10.57) and 80 (70, 85) mmHg. Mean (SD) respiratory rate and pulse rate was 20.83(3.37) and 85.24(9.23). 10% of the subjects had raised JVP. 5% of the subjects had positive ANA (Anti-Nuclear Antibody) profile. 39% of the patients had anterior wall MI and 27% of the subjects had NSTEMI on ECG. On echocardiography 49% had Anterior wall MI, 29% had inferior wall MI, 7% of subjects had global hypokinesia & 10% had no RWMA (Regional wall motion abnormality). 48% of the subjects had grade1 LVDD (left ventricular diastolic dysfunction) & 39% had grade 2 LVDD on echocardiography. Mean LVEF (left ventricular ejection fraction) was 46.81% (7.44). Our study shows that the proportions of subjects with significant LMCA stenosis, LAD stenosis, LCX stenosis and RCA stenosis on coronary angiography were 11%, 61%, 28% and 34% respectively. In this study none of the background variables e.g., age, BMI, hypertension, diabetes, dyslipidemia, Family history of AMI, NYHA class at presentation and ANA profile of the study subjects were significantly associated with LMCA stenosis. Table 1 shows that Dyslipidemia and Family history of AMI were significantly associated with Left Anterior Descending Coronary Artery (LAD) stenosis on coronary angiography.

Table 1: Distribution and association of background variables of study subjects with Left Anterior Descending Coronary Artery (LAD) stenosis on coronary angiography (n=100)

Background variables	LAD stenosis		χ^2 value	df	P-value
	Non-significant	Significant			
Age					
30-40	20 (40.8)	29 (59.2)	0.133	1	0.715
41-50	19 (37.3)	32 (62.7)			
BMI					
Normal	17 (41.5)	24 (58.5)	4.323	2	0.115
Overweight	15 (50)	15 (50)			
Obese	07 (24.1)	22 (75.9)			
Hypertension					
No	17 (41.5)	24 (58.5)	0.177	1	0.674
Yes	22 (37.3)	37 (62.7)			
DM					
No	17 (32.1)	36 (67.9)	2.273	1	0.132
Yes	22 (46.8)	25 (53.2)			
Dyslipidemia					
No	15 (27.8)	39 (72.2)	6.214	1	0.013
Yes	24 (52.2)	22 (47.8)			
Family history of AMI					
No	23 (30.7)	52 (69.3)	8.757	1	0.003
Yes	16 (64)	09 (36)			
NYHA class					
1	29 (42)	40 (58)	0.858	1	0.354
2	10 (32.3)	21 (67.7)			
ANA profile					
Negative	36 (37.9)	59 (62.1)	0.976	1	0.323
Positive	03 (60)	02 (40)			

Table 2: shows that age, BMI, diabetes, dyslipidaemia, Family history of the study subjects were significantly associated with Right Coronary Artery (RCA) stenosis on coronary angiography.

Table 2: Distribution and association of background variables of study subjects with Right Coronary Artery (RCA) stenosis on coronary angiography (n=100)

Background variables	RCA stenosis		χ^2 value. df, p value
	Non-significant	Significant	
Age			7.910, 1, 0.005
30-40	39 (79.6)	10 (20.4)	
41-50	27 (52.9)	24 (47.1)	
BMI			9.766, 2, 0.008
Normal	20 (48.8)	21 (51.2)	
Overweight	22 (73.3)	08 (26.7)	
Obese	24 (82.8)	05 (17.2)	
Hypertension			1.592, 1, 0.207
No	30 (73.2)	11 (26.8)	
Yes	36 (61)	23 (39)	
DM			8.816, 1, 0.003
No	42 (79.2)	11 (20.8)	
Yes	24 (51.1)	23 (48.9)	
Dyslipidemia			0.023, 1, 0.879
No	36 (66.7)	18 (33.3)	
Yes	30 (65.2)	16 (34.8)	
Family history of AMI			10.042, 1, 0.002
No	56 (74.7)	19 (25.3)	
Yes	10 (40)	15 (60)	
NYHA class			0.444, 1, 0.505
1	47 (68.1)	22 (31.9)	
2	19 (61.3)	12 (38.7)	
ANA profile			2.711, 1, 0.100
Negative	61 (64.2)	34 (35.8)	
Positive	05 (100)	-	

Mean LVEF was significantly lower (p value-0.034) and mean LA (left atrial) Diameter was significantly higher (p value-0.004) with subjects with significant LMCA stenosis. On the other hand none of the echocardiography findings were significantly associated with LCX stenosis on coronary angiography. Mean LVESV (left ventricular end systole volume) (p value-0.011), mean LA Diameter was significantly higher (p value-0.004) and mean LVEF was significantly lower (p value-0.009) with subjects with significant LAD stenosis on coronary angiography (Table 3).

Table 3: Distribution and association of Echocardiography findings and Coronary Artery (LAD) stenosis on coronary angiography of study subjects (n=100)

Echocardiography findings	LAD stenosis on coronary angiography Mean (SD)		p value*
	Non-significant	Significant	
LVEDV	114.62 (21.74)	117.84 (15.63)	0.392
LVESV	57.51 (14.43)	63.48 (10.38)	0.011
SV	57.10 (14.20)	54.69 (14)	0.181
LVEF	48.72 (7.36)	45.59 (7.29)	0.009
LA Diameter (mm)	31.05 (2.92)	32.15 (2.64)	0.024

Mean LVEDV was significantly lower (p value-0.032) with subjects with significant RCA stenosis on coronary angiography.(Table 4)

Table 4: Distribution and association of Echocardiography findings and Coronary Artery (RCA) stenosis on coronary angiography of study subjects (n=100)

Echocardiography findings	RCA stenosis on coronary angiography Mean (SD)		p value*
	Non-significant	Significant	
LVEDV	118.77 (16.10)	112.32 (21.38)	0.032
LVESV	62.24 (10.78)	59.03 (15.02)	0.200
SV	56.83 (14)	53029 (14.09)	0.115
LVEF	46.97 (7.50)	46.50 (7.41)	0.574
LA Diameter (mm)	31.42 (2.87)	32.29 (2.57)	0.105

*Parametric or non-parametric tests were done

Discussion

The present descriptive observational study was conducted over one year duration among randomly selected 100 pre-menopausal women with Acute Coronary Syndrome admitted in cardiology ward and intensive coronary care unit of a tertiary care Hospital, West Bengal. The overall aim of the study was to evaluate the clinico-epidemiological and coronary angiographical profile of pre-menopausal women with acute coronary syndrome in a tertiary care hospital.

The clinical parameters, demographic data and echocardiographic findings were collected for all the patients. A detailed history of symptoms was recorded. Details of underlying cardiac disease, blood pressure, and fasting blood glucose and serum lipid profile were measured. The conventional coronary risk factors including age, diabetes mellitus (DM), hypertension, hypercholesterolemia, smoking obesity, family history of CAD and physical inactivity were recorded.

Studies have consistently shown that young women presenting with ACS have significantly greater comorbidities than young men, including smoking, diabetes, metabolic syndrome, hypertension, and chronic kidney disease.¹⁴⁻¹⁷

Coronary angiography was performed on each patient selected according to inclusion and exclusion criteria.

Among the study population 17% of the women were in the age group of 30-35 years, 32% were in between 36-40 years, 28% in 41-45 years and 23% in 45-50 years of age group. The mean ($\pm$ SD) age of the study population was 41.10 ($\pm$ 5.002) years

Among the study population 30% of the subjects were overweight and 29% were obese.

In this study majority (59%) of the women were hypertensive. The mean (SD) and median (IQR) systolic blood pressure (SBP) was 122.12 (19.28) mmHg and 120 (104.25, 130) mmHg; and the diastolic blood pressure (DBP) was 79.72 (10.57) and 80 (70, 85) mmHg. The most common modifiable risk factor for ASCVD (Atherosclerotic Cardiovascular Disease) is hypertension and it is estimated to occur in 85.7 million adults in the United States (44.9 million women and 40.8 million men).¹⁸ Oral contraceptive (OCP) use is associated with increases in

BP and risk of cardiovascular events, which are generally reversible with discontinuation of the OCP.¹⁹

Among all 47% of the subjects were having Diabetes mellitus.

46% of the subjects among study population were having Dyslipidemia.

Obesity and diabetes are increasing in adults in both men and women.²⁰ Astonishingly the age-adjusted prevalence of metabolic syndrome has been reported to fall in women between 1999 and 2010 (with a peak in 2001–2002), but there has been an increase in the prevalence of hypertriglyceridemia and increasing waist circumference due to decreasing physical activity, food habit and decrease sleep duration.²¹

In the study 25% of the subjects were having Positive Family history of AMI.

31% of the subjects belonged to class 2 of NYHA at presentation and rest were in NYHA class1.

Among study population 10% of the subjects had raised JVP(Jugular venous pressure) due to various causes.

Among all the patients 39% of the patients had anterior wall MI and 27% of the subjects had NSTEMI, 25% had inferior wall MI, 4% had lateral wall MI on ECG. 5% patients had no ST-T changes.

In a study it is seen that women presented less often with STEMI than men (50% vs 57%, $p=0.007$), but they were associated with higher rates of Global Registry of Acute Coronary Events (GRACE) score ≥ 140 (19% vs 12%, $p=0.007$).²²

In echocardiographic evaluation 49% had Anterior wall MI, 29% with Inferior wall MI, 7% had global and 5% had lateral wall hypokinesia and 10% had no regional or global wall motion abnormality. Among the young female patients only 5% of the subjects had positive ANA profile. Ischemic heart disease is a common complication of systemic lupus erythematosus (SLE) and may be observed in up to 16% of SLE patients.²³ The most common underlying aetiologies of acute myocardial infarction (AMI) in SLE patients include coronary atherosclerosis, thrombosis, arteritis, and myocarditis.

The mean and median stroke volume were 55.63 and 52 respectively among the study population.

The mean EF was 46.81 and median EF was 46.

48% of the subjects had grade 1 and 39% had grade 2 LVDD on echocardiography.

In this study proportions of subjects with significant LMCA stenosis, LAD stenosis, LCX stenosis and RCA stenosis on coronary angiography were 11%, 61%, 28% and 34% respectively.

In a VIRGO sub-study, patients were grouped according to the type of MI using the third universal definition;²⁴ while most patients had plaque-related MI (82.5% women, 94.9% men), other types included obstructive disease with (1.4% women; 0.9% men) and without (2.4% women; 1.1% men) supply demand mismatch, non-obstructive disease with (4.3% women; 0.8% men) and without supply demand mismatch (7.0% women; 1.9% men), other mechanisms for MI (1.5% women, 0.2% men), and unexplained MI (0.8% women, 0.2% men)²⁵

Background variables e.g., age, BMI, hypertension, diabetes, dyslipidemia, Family history of AMI, NYHA class at presentation and ANA profile of the study subjects were not significantly associated with LMCA stenosis but Dyslipidemia and Family history of AMI were significantly associated with Left Anterior Descending Coronary Artery (LAD) stenosis and NYHA class at presentation was significantly associated with Left Circumflex Coronary Artery (LCX) stenosis and age, BMI, diabetes, dyslipidemia, Family history of the study subjects were significantly associated with Right Coronary Artery (RCA) stenosis on coronary angiography.

In our study mean LVEF was significantly lower (*p value-0.034*) and mean LA Diameter was significantly higher (*p value-0.004*) with subjects with significant LMCA stenosis and mean LVESV (*p value-0.011*), mean LA Diameter was significantly higher (*p value-0.004*) and mean LVEF was significantly lower (*p value-0.009*) with subjects with significant LAD stenosis on coronary angiography. RCA stenosis was associated with significantly lower mean LVEDV (*p value-0.032*).

Limitation

Our study had small sample size. So larger study is required to confirm the findings of our study. This study was descriptive observational study, the study participants were not followed up, and so response to treatment could not be assessed so necessitating the need for prospective longitudinal studies.

Conclusion

AMI incidence is in rising in young female in India. The present descriptive observational study was conducted over one year duration among randomly selected 100 pre-menopausal women with Acute Coronary Syndrome. Anterior Wall MI was the most common presentation in our study. Obesity, hypertension, diabetes, dyslipidemia were important risk factors & 5% of the subjects had positive ANA profile in this study.

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