Retrospective Study Of Common Prevalent Risk Factors Among Female Patients Presented With Acute Coronary Syndrome

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Abstract: **Background and Objective** : Acute coronary syndrome (ACS) is characterized by classical history of ischaemic chest pain, apprehension and sweating with definite Electro-Cardio gram (ECG) evidence or cardiac marker of ischaemia. The risk factors for Coronary Artery Disease (CAD) are modifiable and non-modifiable. CAD is a major cause of disability and the leading cause of death in women. The objective of our study was to assess the impact of various risk factors in women presented with ACS. **Method:** A total of 100 female patients of ACS and twenty healthy females were taken as control. The mean age of women presented with ACS was 62.62 years and all have attained menopause. **Result:** The prevalence of major risk factors of ACS in women are hypertension (78%), stress (74%), obesity (46%), sedentary habits (38%), genetic predisposition (36%), diabetes (32%) and tobacco use (18%),higher socio-economic status (74%). Significantly ($P <0.05$) high levels of total cholesterol, triglycerides along with reduced High Density Lipid (HDL). **Conclusion:** The prevalence of C - reactive protein (CRP) Positivity (>6 mg/L) is significant in women with (92%) as compared to healthy women (20%).[Jain S NJIRM 2014; 5(3) :27-32]

Key Words:Coronary artery disease (CAD), Acute Coronary Syndrome (ACS), Hypertension, Diabetes, Obesity, Hypercholesterolemia, C-Reactive Protein (CRP)

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Introduction: In India, coronary artery disease is one of the most common causes of death. India is home to a quarter of the world's coronary artery disease burden besides having a substantial residual prevalence of pre- transitional cardiovascular disease like rheumatic heart disease.[1,2,3] Only few data are available on Coronary Artery Disease (CAD) in females from our country.[1,4]The traditional and well-studied risk factors for CAD in men namely hypertension, diabetes mellitus , hypercholesterolemia , cigarette smoking , family history of premature CAD, obesity,socio-economic and other personal factors appears to be operative in women also. However women may have a different relative importance of these risk factors and additional factors, such as hormonal status etc. are equally predictors of CAD in women.[1,3]In the Framinghtan study, it was found that the same risk factors appear to be operative in women as in men. Some of these risk factors are modifiable, others immutable (Table A). Presence of any one of the risk factors places an individual at a high risk of CAD , the greater the number of risk factors present the more likely one is to develop CAD.[3,5]

A strong association between blood pressure level and CAD had been reported in prospective studies in women. Anti-hypertensive therapy may reduce both overall morbidity and mortality of CAD as well as the incidence of stroke and these effects are most striking in the elderly.[6,7]

Table A: Risk Factors For CAD In Women

Modifiable	Non-modifiable
High Blood Pressure	Age
Elevated Serum Cholesterol	Sex
Diabetes Mellitus	Family History
Obesity	Genetic Factors
Cigarette Smoking	
Stress	
Sedentary Habits	

Level of blood cholesterol is a strong risk factor for CAD in men and women. Studies have shown that there is a consistent, strong, positive, continuous and graded relationship between plasma total cholesterol and the incidence of CAD.[8,9,10] In women, high HDL levels are particularly strong predictors of lower CAD risk. HDL cholesterol is strongly and inversely related to number of cigarettes smoked per day among smokers, triglycerides level and body mass index. Hypertriglyceridemia patients often manifest hypertension, hyperinsulinemia, visceral obesity and impaired glucose intolerance along with

precoagulated state and atherogenic lipoprotein phenotype, a very high risk state for CAD.[11] Diabetes Mellitus (DM) is a stronger coronary artery disease risk factor in women than in men. Diabetes adversely influences the favourable CAD experience of women compared to men. Diabetes exacerbates the effects of other risk factors also.[1,2,12,13] Diabetes mellitus-II is associated with obesity, hypertension and insulin resistance , all of which have been associated with higher CAD risk. Diabetes is also linked with presence of hyperlipidemia, especially in women.[14] There is a strong positive association between obesity and the risk of CAD in women as demonstrated in Harvard medical school women's hospital. [15] The risk of CAD was over three times higher in women with a body mass index (BMI) of 29 and above compared with women with a BMI of less than 21. The excess risk could be attributed to effects of obesity on blood pressure, glucose intolerance and lipid levels.[16] Smoking risk is significantly synergistic with that of oral contraceptives use, especially in women over age 35 years and leads an early menopause, another CAD risk unique to women.[17,18] In Nurses' Health study , in comparison with non-drinkers , women who consumed 10-15 Gm of alcohol per day had a 40% lower risk of CAD.[19] Findings from case control analysis in the Boston Area Health study indicate that alcohol raises HDL and reduces platelet aggregation.[20] Women have been shown to improve their cardiovascular risk profiles with increasing levels of physical activity and physical fitness.[21] Epidemiological studies found an increased risk of CAD in current users of the combined oral contraceptive pills. The relative risk of admission for myocardial infarction in women who had been using oral contraceptives in the previous month compared with that in women who had never used them is estimated to be 4.5 to 1.[22,23] Studies suggest a complex relationship between CAD risk, estrogen, menopause and serum cholesterol in women. Menopause is associated with adverse effects of lipid profile in women. National cholesterol Education programme guide lines suggest hormone replacement therapy for primaryprevention and lipid lowering in post-menopausal women.[24,25]Estrogen has been demonstrated to have beneficial effects on a range of cardiovascular risk factors. Most noticeably they increase HDL- Cholesterol and lower LDL-Cholesterol and plasma levels of plasminogen activator inhibitor for type-I (PAI-1) which inhibits fibrinolysis.[22,26]Serum CRP level increases within 4-6 hours after an acute tissue injury and sharp increase in serum CRP level accompanies myocardial infarction.[27,28]Studies suggest that CRP is a strong independent risk factor for CAD.[29]

Material And Methods: Following approval from institutional ethical committee, this retrospective study was done in 100 female cases of ACS admitted in Medical ICU from March 2013 – November 2013. The diagnosis of acute coronary syndrome made according to the world Health Organization (WHO) recommendation.[30]

The Patient is said to have acute myocardial infarction if she fulfilled atleast two of the following three criteria:
- History of characteristic severe ischaemic chest pain of atleast 30 minutes duration, typically retrosternal in location, spreading frequently to both sides of anterior chest, with predilection for left side, unresponsive to sublingual administration of isosorbide dinitrate.
- Evolutionary changes in serially obtained ECG tracing more commonly new ST segment elevation more than 2 mm persisting more than 20 msec, after J point in atleast two standard surface ECG leads with or without reciprocal changes and pathological Q- waves.
- If ECG is not showing MI but there is a clinical suspicion and MI is proved by rise of serum cardiac markers, more so of MB isoenzyme fraction of creatine kinase (CK-MB) which is more specific in diagnosing acute myocardial infarction.

Localization of MI was done on the basis of ECG patterns.[31]Twenty healthy female in the age group of forty plus in whom ACS were excluded on the basis of clinical history, examination, routine ECG, were taken as control. The present study had two groups: Study group: Group-I (N=100) female with ACS and Control group: Group-II (N=20) female

without ACS. Study protocol included detailed clinical history, clinical examination and investigations. In the present study, patients were examined based on age, rural or urban, occupation and the physical work associated, chronic stress, regular aerobic exercise, socio- economic status, monthly income, smoking, tobacco chewing or doing tobacco paste, alcohol consumption with special reference to menstrual history. Patients were also evaluated for past history of hypertension, CAD, diabetes mellitus and CVA including duration and regularity of treatment. Family history of hypertension, CAD, diabetes mellitus and CVA, obesity, sudden death and hyperlipidemia were also enquired about. BMI, vitals and CVS examination were done.

Socio- economic status of the patients were divided into four classes on the basis of income in rupees per year[32]: (a)Lower class (L) annual income up to Rs. 40,000 per annum (b) Lower middle class (LM) annual income Rs. 40,000 –Rs. 1.5 lakh per annum (c) Upper middle class (UM) annual income Rs. 1.5 lakh – Rs. 3.0 lakh per annum (d) High class (H) annual income >Rs3.0 lakh per annum.

Subjects were asked about duration of tobacco intake and amounts consumed and were divided in two groups, tobacco chewer and non-tobacco chewer. Cases were asked about duration, no. of cigarettes/bidis smoked per day and were divided into four groups[18], (a) non-smoker, (b) light smoker 1-14 cigarettes /day (c) moderate smoker 1-24 cigarettes / day (d) heavy smoker >25 cigarettes / day. Patients were divided in to non-obese and obese on the basis of body mass index (BMI). A BMI of 27.3 Kg/m^2 or more in female indicates obesity[18]

BMI=$\dfrac{\text{Body weight (Kg)}}{\text{Height}^2 \text{(m)}}$

Results: The present study was done on 100 female patients with acute coronary syndrome (ACS) admitted in ICU of SRG Hospital and medical College Jhalawar and comparing them with twenty healthy control female subjects who have attained

their menopause and in whom CAD was excluded on the basis of clinical history and routine ECG.

The mean age of females with CAD was 62.62 years and ranged between 44 and 80. In control group the mean age was 57.70 years with a range of 44 to 72 years.

Table 1: Mean Age Distribution Of Study Subjects

	Case (n=100)	Control (n=20)
Mean age (years)	62.62	57.70
Range	44-80	44-72

ACS is more prevalent in urban (62%) while less in rural population (38%).In control group 70% of population is from rural area.

Table 2:Rural/Urban Distribution Of Study Subjects

Rural/Urban	Case (n=100)		Control (n=20)	
	No.	%	No.	%
Rural	38	38.00	14	70.00
Urban	62	62.00	6	30.00

Among 100ACS patients genetic predisposition was observed in 36 percent. The major risk factors in the study group were hypertension (78%), stress (74%), lack of physical exercise (38%), diabetes (32%) and tobacco consumption (18%). Stress (65%) and sedentary habits (30%) were prevalent in the control group

Table 3: Coronary Risk Factors Profile In Females

Risk factors	Case (n=100)		Control (n=20)	
	No.	%	No.	%
Family history of CAD	36	36.00	0	0.00
Hypertension	78	78.00	1	5.00
Diabetes mellitus	32	32.00	0	0.00
Sedentary habits	38	38.00	6	30.00
Stress	74	74.00	13	65.00
Tobacco smoking	4	4.00	0	0.00
Tobacco chewing	14	14.00	1	5.00

Forty percent of patients were belonging to high socio- economic group while 34% from upper middle class and 26% from lower socio- economic strata. In control group 40% each were belonging

to high socio –economic status and lower middle class while 15% were from upper middle category .

Table 4: Clinical Correlation Of Socio-Economic Status Of Females With And Without ACS

Socio-economic status	Case (n=100)		Control (n=20)	
	No.	%	No.	%
Lower (<40,000/annum)	6	6.00	1	5.00
Lower middle (40,000-1.5 lakh/annum	20	20.00	8	40.00
Upper middle(1.5-3.0 lakh/annum)	34	34.00	3	15.00
High (> 4 lakh)	40	40.00	8	40.00

The majority of females achieving menopause around 50 years of age and substantially more. However, those who had early menopause (≤ 40 years) also developed the disease (10%).

Table 5: Onset Of Menopause And Prevalence Of ACS

Age of menopause	Case (n=100)		Control (n=20)	
	NO.	%	No.	%
≤ 40 years	10	10.00	0	0.00
41-50 years	52	52.00	16	80.00
> 50 years	38	38.00	4	20.00

In the control group only 10% women who presented with obesity while females with ACS had higher incidence (46%) of obesity. Moreover 90% of control group had normal BMI.

Table 6: Association Of Body Mass Index With ACS

BMI (kg/m^2)	Case (n=100)		Control (n=20)	
	No.	%	No.	%
< 27.3 (Non-obese)	54	54.00	18	90.00
>27.3 (Obese)	46	46.00	2	10.00

92 % of females with ACS, CRP value >6mg per l while only 20% of females from control group crossed this value.

Only serum cholesterol levels are statistically significant (p<0.05) in women with ACS as compared to control. Rest of the lipid fractions and

cholesterol/HDL ratio is statistically not significant (P=NS) .

Table 7: Correlation Of C-Reactive Protein (CRP) In Females With And Without ACS

CRP (mg/l)	Case (n=100)		Control (n=20)	
	No.	%	No.	%
<6	8	8.00	16	80.00
>6	92	92.00	4	20.00

Table 8: Lipid Profile Pattern In Females With And Without ACS

Lipid profile	Cases (n=100) Mean ± SD	Control (n=20) Mean ± SD	P value
Cholesterol(mg/dl)	168.84±47.85	144.80±37.87	<0.05
Triglyceride(mg/dl)	149.94±80.55	128.50±50.94	NS*
HDL-C (mg/dl)	55.84±26.39	50.70±16.86	NS*
LDL-C (mg/dl)	86.00±43.60	68.40±35.60	NS*
VLDL-C (mg/dl)	29.99±16.11	25.70±10.19	NS*
Serum TC/HDL	3.58±1.469	3.037±0.8574	NS*

*NS= Not significant

Hypertriglyceridemia, raised serum levels of LDL-C and VLDL-C are more prevalent in females with ACS than control group and all are statistically significant (P<0.05). Prevalence of low serum HDL-C (<35mg/dl) and high C/HDL- C ratio (>5) are not showing statistically significant (P=NS).

Table 9: Dyslipidemia In Females With And Without ACS

	Cases (n=100)		Control (n=20)		P value
	No.	%	No.	%	
Hypercholesterolemia (>200mg/dl)	26	26.00	1	5.00	<0.05
Hypertriglyceridemia (>150mg/dl)	39	38.00	3	15.00	<0.05
HDL-C(<35mg/dl)	26	26.00	4	20.00	NS*
LDL-C (>130mg/dl)	10	10.00	0	0.00	<0.05
VLDL-C (730mg/dl)	38	38.00	3	15.00	<0.05
TC/HDL-C(75)	14	14.00	1	5.00	NS*

*NS =Not significant

Discussion: The coronary artery disease is one of the common diseases of women in old age

(Specially Post-menopause). This study is done to assess the impact of various risk factors among women from acute coronary syndrome. The work is based on the study of 100 female patients in MICU with acute coronary syndrome (ACS) and comparing them with 20 healthy control subjects who have their menopause and in whom coronary artery disease has been excluded on the basis of clinical history and routine electrocardiogram (ECG). The mean age of women presented with ACS was 62.22 years in our study, more or less similar to study reported earlier.[1,14,33,34] The incidence of ACS is more in urban (62%) than rural (38%) population, approximately similar observations reported by Gupta and associates.[35] A lesser degree of physical activities, increased body mass index (BMI), and higher frequency of hypertension and diabetes amongst the urban community are some of the factors responsible for difference in incidence.

Coronary risk factors in 100 female patients of ACS revealed that major risk factors are hypertension (78%), stress (74%), sedentary habits (38%), genetic predisposition (36%), diabetes (32%) and tobacco consumption (80%). The control group analysis for coronary risk factors revealed hypertension 5%, consumption of tobacco 5%, obesity in 10%, sedentary habits in 30% and chronic stress in 65%. Diabetes was not detected in any of the control subjects. It was observed that 74% of women were belonging from higher socio-economic strata and only 26% from lower. Studies have shown that people engaged in heavy work such as farm laboring had a lower prevalence of CAD than people with sedentary habits.

In our study none of the women with ACS presented before menopause, similar to the Balakrishnan study.[36] Only 10% of women presented with early menopause (≤ 40years). Obesity (BMI ≥ 27.3) was 4.6 times more common in women with ACS than in control group, Manson and associate in nurses Health study found increase risk of CAD in women having obesity. Obesity worsens several coronary risk factors, including hypertension, diabetes and hypercholesterolemia and thought to be a predictor of CAD. 32% of patients presented with diabetes mellitus, an important risk factor for CAD in women than men. 26 % patients presented with hypercholesterolemia and the difference is statistically significant (P<0.05) as compared to the control. The role of serum TG continues to be debated as a ACS risk factors. In Indians commonly observed lipid pattern is average cholesterol with relatively high TG level and low HDL-C. In our study prevalence of hypertriglyceridemia is significantly (P<0.05) more common in women with CAD than in control. It appears that CRP may prove to be the strongest and most significant predictor of the risk of future coronary events. Similarly in this study it has been observed that 92% of cases had CRP value more than 6 mg/l but only 26% of cases presented with hypercholesterolemia and only 38% cases presented with hypertriglyceridemia. These data raise the possibility that the addition of CRP levels to standard lipid screening will generate an improved method for identifying persons at higher risk of CAD.

Conclusion: This study shows that the major risk factors for acute coronary syndrome in post-menopausal females are hypertension, stress, obesity, genetic predisposition, diabetes, tobacco use and sedentary life styles. Modifiable risk factors such as hypertension, obesity, stress, sedentary life style and tobacco use can be controlled by dietary restrictions, exercise, lifestyle changes and use of anti-hypertensive medication and can effectively decrease the acute coronary syndrome in females also.

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