

Original Research Article

Clinical profile of premenopausal female patients with coronary artery disease

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Received: 23 May 2018

Accepted: 28 May 2018

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ABSTRACT

Background: Coronary artery disease is becoming the leading cause of death in the world. The incidence of CAD in females has increased rapidly in the past decades. This study aimed to analyze the clinical profile of premenopausal women with CAD and elucidate on the possible risk factors.

Methods: Premenopausal female patients admitted with an acute coronary syndrome as diagnosed by history, ECG and laboratory tests were recruited. Clinical and biochemical parameters were recorded.

Results: Mean age of study participants was 41.6 ± 8.18 yrs. Unstable angina (60%) was the most common clinical presentation. Proportion of women with various risk factors of CAD in our study population were as follows: dyslipidemia (65%), family history of premature CAD (57.5%), hypertension (55%), diabetes mellitus (42.5%), hypothyroidism (40%), PAD (37.5%), CKD (35%) and SLE (20%). Most (95%) of the study population had high LDL-c. Three fourth (77.5%) of the study population had low HDL. Approximately half of the study population had fatty liver on ultrasonography. Triglyceridemia was found in 72.5% of the study population.

Conclusions: Premature CAD is increasingly evident in young premenopausal women in India. Premenopausal CAD in India is of multi factorial causation and dyslipidemia, hypertension, diabetes mellitus, central obesity and family history of premature CAD play a crucial role in its development.

Keywords: Coronary artery disease, Premenopausal women

INTRODUCTION

It is well-known that coronary artery disease (CAD) is becoming the leading cause of death in the world. CAD has generally been considered as a disease of middle-aged men. The incidence of CAD in females has increased rapidly in the past decades.

CAD in the female population especially in premenopausal women is still identified less often and sensitively and is treated less aggressively than that in the male population. Even now, there are still less detailed data to describe the characteristics, mechanisms and prognosis of premenopausal CAD patients. This study

aimed to analyze the clinical profile of premenopausal women with CAD and elucidate on the possible risk factors.

Globally, CAD is the leading cause of death and is predicted to remain so for the next 20 years.¹ According to the Global burden of disease study developing countries contributed 3.5 million of the 6.2 million global deaths from CHD in 1990.² The CVD burden afflicts both men and women, with CVD accounting for 34% of all death in women and 28% in men in 1998.³ As the epidemic advances, the social gradient also reverses with the poor becoming the most vulnerable victims in both developed and developing countries.⁴ Annual CHD

population statistics continue to report a greater, number of deaths for women than men (455,000 vs. 410,000).⁵ The most recent Centres for Disease Control and Prevention data reveal that 1 in 2.6 women die from CHD.⁶

In addition to an absolute greater number of women dying from CAD, a greater proportion of women die of sudden cardiac death before their arrival at a hospital (52%) contrasted with 42% of men.^{7,8} Recent data report significant decreases in sudden cardiac death in men with essentially no change in women.⁹ The first MI attack occurs in 4.4% of Asian women and 9.7% of men at age less than 40 years, which is 2 to 3.5. fold higher than in the West European population and is third highest of all the regions studied worldwide.¹⁰ Younger Asian women have worse survival at 28 days after acute MI.^{11,12} In view of the above discussion, it is imperative to ascertain the causes of the rising prevalence and emergence of CAD earlier in the life of Indians.

More than 80% of midlife women have one or more traditional cardiac risk factors.¹³ Women have, on average, greater blood cholesterol levels than men after their fifth decade of life and exhibit mild decreases in high density lipoprotein cholesterol after menopause.¹⁴⁻¹⁶ Obesity is prevalent in one-third of women, including 7% having a body mass index of 40kg/m² with associated increased mortality.^{17,18} Hypertriglyceridemia is a more potent independent risk factor for women as compared with men.^{19,20} Diabetic women has significantly greater rates of IHD mortality compared with diabetic men and an elevated 3.3 fold IHD risk compared with nondiabetic women.²¹⁻²³

The rate of IHD mortality increases with the number of traditional cardiac risk factors, with 30-year death rates per 10,000 person years ranging from 1.5 to 9.1 for women with a to 2 risk factor clustering of risk factors is common after menopause, notably the combination of obesity hypertension, and dyslipidemia.²⁴⁻²⁶ This phenomenon is potentially related to hormonally-mediated metabolic disturbances. As the prognosis in women is worse than that of men, these facts underline the need for giving special attention to women and heart disease. Informing women about their risk factors will help them to respond in a better way to preventive health advice and will enable them to recognize symptoms themselves.

METHODS

Study design

Descriptive study of one-year duration in 40 premenopausal female patients admitted in the wards under the Departments of General Medicine and Cardiology at Government T. D. Medical College Hospital, Alappuzha.

Inclusion criteria

The study includes all premenopausal female patients admitted with an Acute Coronary Syndrome as diagnosed by history, ECG and laboratory tests (CKMB, Troponin levels) in medical wards at Government T.D Medical College Hospital, Alappuzha during the afore mentioned period.

Exclusion criteria

Study exclusion criteria included pregnancy, cardiomyopathy, New York Heart Association functional class IV, valvular heart disease and those not willing for study. Postmenopausal women and those with indeterminate menopausal status were not included in the present analysis.

Criteria to diagnose CAD

- History of typical cardiac chest pain,
- ECG changes suggestive of ischemia CKMB elevation (more than 3 times the baseline) with or without a positive troponin 1,
- Echocardiography.

This is an observational study of all premenopausal female patients admitted with an acute coronary syndrome diagnosed by history, ECG and laboratory tests (CKMB, troponin levels) in accordance with the inclusion criteria mentioned above.

Informed consent was obtained following which the patients were subjected to a detailed evaluation. All patient details were collected using a structured questionnaire.

Patients' name, age, sex, occupation and address were noted. A clinical history focusing on symptoms of chest pain was obtained. A past history of diabetes mellitus, hypertension, dyslipidemia, coronary artery disease, chronic kidney disease, peripheral vaso-occlusive disease, hypothyroidism, systemic lupus erythematosus, polycystic ovary disease, gestational hypertension, gestational diabetes mellitus, intake of oral contraceptive pills, synthetic progestogen and. history pertaining to smoking was elicited. Smoking was defined as use of bidis (bidis are small, hand-rolled cigarettes wrapped in a piece of local tobacco leaf), cigarette or oral tobacco. Consumption of 1g of oral tobacco was taken as equivalent to smoking one cigarette. Family history of CAD also was taken into account. Menstrual history was taken in detail.

They were then subjected to a thorough clinical examination looking for obesity, waist circumference, body mass index, acanthosis nigricans, skin tags, diminished peripheral pulses, and blood pressure measurement. Cardiovascular examination was done to look for presence of cardiomegaly, S3, S4 and bruits.

A blood routine, fasting blood sugar, renal function tests, liver function tests, fasting lipid profile, thyroid function tests were done.

USG abdomen was obtained. An echocardiogram was done to assess the left ventricular ejection fraction and to look for wall motion abnormalities, diastolic dysfunction, chamber enlargement. Ankle-brachial index and carotid intima medial thickness could not be assessed as the machine was not functioning.

Risk factors

- Diabetes mellitus-Fasting Blood Sugar: \geq 126 mg/d.
- Hypertension-Blood pressure $>$ 130mm systolic or $>$ 85mm diastolic or on medication for the same.
- Previous history of CAD-Luminal diameter narrowing of \geq 50% in any of the major epicardial coronary arteries was diagnosed as CAD.
- Hypothyroidism -Subclinical -TSH \geq 4.5 IU and \leq 10 IU with normal T4 levels. Overt hypothyroidism if TSH \geq 10 IU with low thyroid hormones.
- PCOS -Defined according to clinical (Ferriman-Gallwey score $>$ 8) oligomenorrhea or amenorrhea \geq 6 months; biological LH/FSH ratio $>$ 2; hyperandrogenism] and ultrasonographic findings.
- Chronic Kidney Disease -Estimated GFR as calculated by MDRD formula \leq 60 ml/min.
- Family History of premature CAD -Definite MI or sudden death before age 55 years in a father or other male first-degree relative, or before age 65 years in a mother or other female first-degree relative.
- Gestational diabetes mellitus- Diabetes detected for the first time during pregnancy till 180 days after delivery.
- Gestational hypertension -BP $>$ 140/90 after 20 weeks of gestation.
- Severe anemia -Hb \leq 8g/dl.

Lipid profile

- S. Triglyceride (Hypertriglyceridemia: $>$ 150mg/dl; or on specific medication),
- HDL value (low HDL: $<$ 50mg/dl or on specific medication),
- LDL value (Elevated if $>$ 100mg/dl).

Statistical analysis

After preparing master chart, the history, clinical findings and laboratory investigations were recorded, and analyzed in terms of frequency and percentage of co-relationship.

The significance of association between history), clinical findings and laboratory investigations were assessed with the help of appropriate biostatistics.

RESULTS

Mean age of study participants was 41.6 years and standard deviation (SD) was 8.18 (Table 1). 62% of study population presented with chest pain. Dyslipidemia was the most common comorbidity occurring in 65% of study population (Table 2). Seventeen (42.5%) of study participants had taken hormonal pills. Tobacco use was found in 20% of our study population (Table 3). Mean BMI was 23.32 and SD was 3.76 (Table 4).

Table 1: Age distribution of premenopausal women with CAD.

Age group	No. of persons	Percentage
21-30	5	12
31-40	14	35
41-50	16	40
$>$ 51	5	13
Total	40	100

Table 2: Medical comorbidities in premenopausal women with CAD.

Comorbidity	Frequency	(%)
Dyslipidemia	26	65
Family history of premature CAD	23	57.5
HTN	22	55
OM	17	42.5
Hypothyroidism	16	40
PAD	15	37.5
CKD	14	35
SLE	8	20
DM and HTN	4	10
Previous CAD	4	10

Table 3: Tobacco usage.

Tobacco usage	Frequency	Percentage
Percentage	8	20
Absent	32	80
Total	40	100

Table 4: Body mass index.

BMI range	Frequency	Percent
$>$ 18.5	6	15%
18.5-24.9	16	40%
25.0-29.9	17	43%
30 and above	1	3%

60% of our study population had a waist circumference of \geq 80cm. Skin tags were found in 20% and *Acanthosis nigricans* in 35.5% of study population (Figure 1).

Mean systolic pressure in premenopausal women with CAD was 150.15mm and SD was 21.46. Mean diastolic BP was 95.05mm and SD was 14.51. Mean hemoglobin

was 9.41 and SD was 1.90 (Figure 2). Mean serum total cholesterol levels were 243.85mg/dl and standard deviation was 35.86 (Figure 3). Mean serum LDL-C was found to be 148.10 mg/dl and standard deviation was 23.51 (Figure 4). Mean serum HDL-C level was 45.60mg/dl and standard deviation was 4.77 (Figure 5).

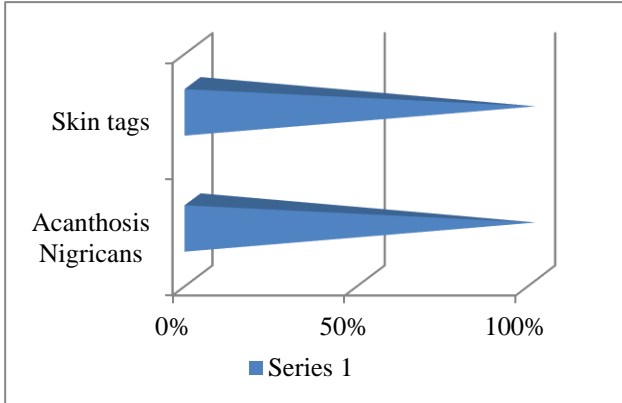


Figure 1: Cutaneous markers of insulin resistance in the premenopausal women with CAD.

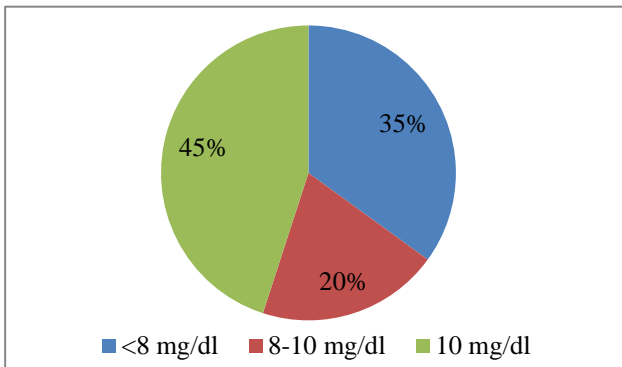


Figure 2: Haemoglobin level.

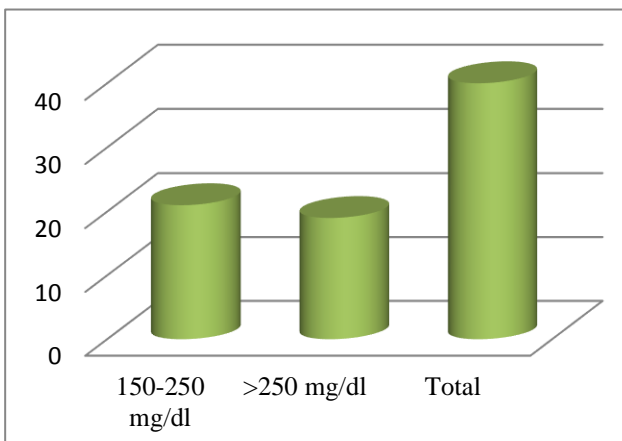


Figure 3: Serum total cholesterol levels in premenopausal women with CAD.

Mean S. triglyceride was 220.58mg/dl and SD was 80.84. Mean fasting blood sugar level was 129.33mg/dl and SD

was 46.05. Mean TSH level was 11.39IU and SD was 15.57.

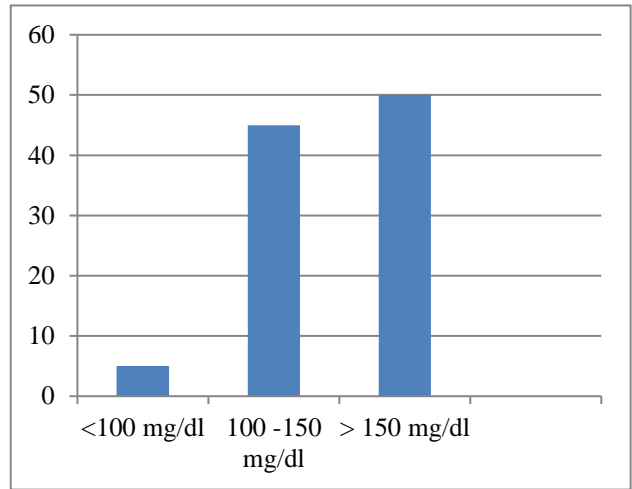


Figure 4: Serum LDL (mg/dl).

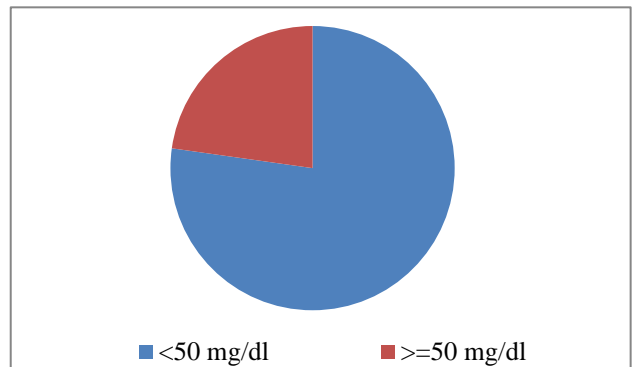


Figure 5: Serum HDL (mg/dl).

DISCUSSION

Forty premenopausal women who presented with ACS were enrolled for this study. The age group ranged from 21 yrs to 55 yrs with the maximum number of patients being in the age group of 41-50 yrs (16, 40%). The mean age of the study participants was 41.6±8.18 years.

Prevalence of various risk factors of CAD in our study was dyslipidemia (65%), family history of premature CAD (57.5%), hypertension (55%), diabetes mellitus (42.5%), hypothyroidism (40%), peripheral arterial disease (37.5%), CKD (35%), SLE (20%), previous CAD (10%) and diabetes mellitus and hypertension (10%).

Our study revealed a high prevalence of dyslipidaemia (65%) i.e. high LDL-C (95%), low HDL-C (77.5%) and significantly higher triglyceridaemia (72.5%) in the study population. In our study, mean HDL was 45.60±4.77, mean LDL was 148.10±23.51, mean serum triglycerides were 45.6±4.77, mean serum total cholesterol was 220.58±80.84. It can be postulated that metabolic profile of patients has deteriorated over time and a possible

explanation could be degradation of lifestyle habits with greater consumption of junk food by the young population.

Twenty percent of our study subjects reported an intake of hormonal pills. Further data on the type of pill and its constitution could not be gathered in the questionnaire due to poor recall by the subject.

Women with diabetes also have a higher incidence of myocardial infarction, and are more likely to die after myocardial infarction, than either men or women without diabetes.²⁷ In this study, 42.5 % of the patients were diabetic. Mean FBS was found to be 129.33mg/dl. The deleterious effect of diabetes on vascular function and, in particular, endothelial function increases the potential for coronary vasoconstriction and thrombosis.^{28,29} Our findings provide direct evidence that premenopausal women with diabetes have a significantly impaired regulation of coronary vascular tone.

Smoking has been shown to be a major dominant modifiable risk factor associated with young CAD.^{30,31} Developing countries like China and India are witnessing an increase in the incidence of smoking, especially among adolescents and a rise in the use of smokeless tobacco.³² Incidence of tobacco usage in the study subjects was 20%. The results indicate that still greater efforts are needed to control smoking among the young and the contribution of passive smoking to the pathogenesis of CAD in premenopausal women has to be studied further. Among the cutaneous markers of insulin resistance, acanthosis nigricans was found in 35% of the study population and skin tags were found in 20% of the women. Severe anaemia was found in 35% of the study population we were not able to further work up the cause for anaemia in those patients.

In our study population, 24 (60%) women were diagnosed with unstable angina, 10 (25%) with NSTEMI and 6 (15%) with STEMI. The most common ECG change in our study was ST segment depression found in 60% of the population. Echocardiographically, LV diastolic dysfunction was the most common finding (53%).

CONCLUSION

Mean age of study population was 41.6±8.18 yrs. Sixty percent of the study population presented with typical chest pain. Unstable angina (60%) was the most common clinical presentation. Proportion of women with various risk factors of CAD in our study population were as follows dyslipidemia (65%), family history of premature CAD (57.5%), hypertension (55%), diabetes mellitus (42.5%), hypothyroidism (40%), PAD (37.5%), CKD (35%) and SLE (20%) about 42.5% of the study population had given history of intake of hormonal pills. Tobacco usage was present in 20% of the study population central obesity was found in 60% of the study

group. Mean BMI was 23.32±3.75. Most (95%) of the study population had high LDL-c' three fourth (77.5%) of the study population had low HDL. Approximately half of the study population had fatty liver on ultrasonography. Triglyceridemia was found in 72.5% of the study population. Hypothyroidism was found in 40% of the study population. Among them 69.5 % had overt hypothyroidism. LV diastolic dysfunction was found in 53% of the study population.

ACKNOWLEDGEMENTS

Authors would like to thank the Biochemistry Department of the Institution who obliged to give the biochemistry reports in time.

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Unnikrishnan KTD, Ambili NR, Mathew D, Renymol B. Clinical profile of premenopausal female patients with coronary artery disease. *Int J Res Med Sci* 2018;6:2285-90.