CLINICAL PROFILE, ANGIOGRAPHIC CHARACTERISTICS IN WOMEN WITH CORONARY ARTERY DISEASE, ADMITTED IN A TERTIARY CARE HOSPITAL OF EASTERN INDIA

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ABSTRACT

BACKGROUND
Women constitute about 48% of the total population in India; however due to inadequate perception and attention, CHD also remains a formidable health problem of women in India and it is rightly said that CHD is under diagnosed, undertreated and under researched disease in women for various reasons. Therefore, this study was designed to determine the clinical profile and angiographic characteristics of women with CAD who presented to our hospital, one of the apex referral centre in eastern part of India.

MATERIALS AND METHODS
One hundred (100) consecutive in-patients from the department of Cardiology were enrolled in this study during the period- October 2015 to October 2017. Ethical committee approval taken from institutional ethics committee. Informed consent from each patient was obtained. Baseline demographics, clinical and risk factor profile were collected. Elective coronary angiography was performed through standard femoral or radial artery approach. Angiographic data were collected by analysing the angiograms by two interventional cardiologists. The Statistical Package for Social Science (SPSS) version 15 was used for data analysis. Categorical data were compared using the chi-square or Fisher's exact test, as appropriate.

RESULTS
Maximum incidence of CAD occurred in age group of > 65 years i.e. 32%, compared to 14%, 28%, 26% in 35-44, 45-54, 55-64 years age group respectively. The most common symptom was chest pain (typical), seen in 100% of patients. The major risk factor in this study was hypertension (50%), diabetes mellitus (34%). We found 60% of patients to be hypercholesterolaemic, 40% were altered triglyceride levels and 40% were having LDL cholesterol of more than 130 mg%. HDL cholesterol of less than 35 mg% was found in 30% of patients. In our study 70% of patients were post-menopausal and only 30% of patients were pre-menopausal with normal cycle. Among post- menopausal women, 30 (42.2%) were diabetic as compared to 8 (26.6%) pre-menopausal women. (P value – 0.126374) Single vessel disease (SVD) was most frequent type of CAD (66%) in young women, whereas it was equally distributed form of CAD in elderly women. (P value – 0.001616).

CONCLUSION
As per our study the mean age of CAD in female in this part of India is smaller as compared to western studies. Women with CAD, from this part of the country suffer more from angina, sweating, vomiting and palpitation and less from shortness of breath. None of the patient in this study presented with syncope. Dyslipidaemia was the most common risk factor found in this study. Postmenopausal females were suffering more from dyslipidaemia as compared to women with normal cycle. (p value - 0.00011) More than 2/3rd of postmenopausal female were suffering from CAD as compared to pre-menopausal counterpart (1/3rd).

KEYWORDS
Women, Coronary Artery Disease, Clinical Profile, Angiography.

BACKGROUND
Coronary heart disease (CHD) is perceived to be of greater importance in men and is largely considered to be a man's disease. It is also the leading cause of mortality and morbidity in middle aged women in developed and developing countries. Women constitute about 48% of the total population in India; however due to inadequate perception and attention, CHD also remains a formidable health problem of women in India and it is rightly said that

CHD is under diagnosed, undertreated and under researched disease in women for various reasons.[1] Coronary manifestations usually appears 10 years later in women as compared to men and myocardial infarction (MI) occurs approximately 20 years later.[2] Hospital mortality from MI is higher in women than in men, a recent study showed hospital mortality of 16.7% for women and 11.5% in men.[3] The unadjusted mortality at 30 days is 13% for women and 4.8% for men and the risk of complication such as shock, heart failure and reinfarction is also more in women.[4] As a preliminary step in the process of discerning these changes, the clinical and angiographic profiles of women undergoing CAG must be understood. There are not many studies describing the prevalence and pattern of "coronary artery disease" (CAD) in women undergoing CAG. Therefore, this study was designed to determine the clinical profile and angiographic characteristics of women with CAD who presented to SCB Medical College Hospital, which is one of the apex referral centre in eastern part of India.

MATERIALS AND METHODS
Selection Criteria
This study is a prospective, observational, hospital-based study. All female patients above 18 years of age admitted in department of cardiology of S.C.B.M.C.H, Cuttack with typical or atypical symptoms, but diagnosed as coronary artery disease by electrocardiogram and/ or cardiac bio-markers and/ or invasive or non-invasive coronary angiogram. Consecutive 100 adult female patients admitted in cardiology department of this tertiary care hospital with signs and symptoms suggestive of IHD were considered for this descriptive observational study. Ethics committee approval was taken for the study.

Inclusion Criteria
Female patients of age greater than 18 yrs. with or without Family history or personal history of Ischemic heart disease, With or without conventional or non-conventional CAD risk factors and along with EKG, biomarkers and/ or imaging evidence of CAD.

Exclusion Criteria
Females with normal EKG, normal bio-markers and normal invasive and/or non-invasive coronary angiogram and patients with chronic kidney disease.

Study Protocol
Cases will be selected on the basis of above inclusion criteria. All the selected patients will be subjected to detailed history, complete physical examination and data collected, will be noted in a predesigned proforma. Relevant investigations such as all routine investigations, EKG, echocardiogram, lipid profile, CRP, specific cardiac bio-markers (Troponin T/I, CK-MB), coronary angiogram.

Study Population
One hundred (100) consecutive in-patients from the department of Cardiology were enrolled in this study during the period from October 2015 to October 2017. Informed consent obtained from each patient. Coronary Artery Disease was defined as presence of stable angina, unstable angina or myocardial infarction. Patients with stable angina were recruited from outpatient department while those of unstable angina and myocardial infarction were recruited from both ward and ICCU department. Baseline demographics, clinical and risk factor profile were collected. Elective coronary angiography was performed through standard femoral or radial artery approach. Angiographic data were collected by analysing the angiograms by two interventional cardiologists. CAD was defined as ≥1 epicardial coronary segment with diameter stenosis > 50% and was diagnosed visually and using quantitative coronary angiography (QCA) software. Patients were grouped as having single vessels disease (SVD), double vessel disease (DVD) and triple vessel disease (TVD) according to the number of vessel involvement.

Statistical Analysis
The Statistical Package for Social Science (SPSS) version 15 was used for data analysis. Results were expressed as mean and frequencies (percentages) for categorical variables in the form of tables. Categorical data were compared using the chi-square or Fisher's exact test, as appropriate and P significance accepted if value < 0.05.

RESULTS
In our study, the minimum age of women with CAD was 35 years and the maximum was 74 years. The mean age of presentation was 57 years. Maximum incidence of CAD occurred in age group of > 65 years i.e. 32%, compared to 14%, 28%, 26% in 35-44, 45-54, 55-64 years age group respectively (Table 1). In our study of 100 female patients with IHD, all patients (100%) had typical chest pain. Vomiting was seen in 60% of patients, followed by sweating (40%), palpitation (34%), and the least common symptom was shortness of breath (12%) (Table 2). The major risk factor in this study was dyslipidaemia (62%), hypertension (44%), diabetes mellitus (36%). The other major risk factor was family history of IHD (24%), Hypothyroidism (11%) of patients. 2% of our study patients were on chemotherapy (CHOP regimen) for Hodgkin's lymphoma. As smoking incidence among female in this region is very low, none of our patients were found to be current or past smoker. None of the patients were on HRT or OC pill or suffering from PCOD (Table 3). Among study patients, 62% of them were found to be hypercholesterolaemic, 36% were altered triglyceride levels and 42% were having LDL cholesterol of more than 130 mg%. HDL cholesterol of less than 35 mg%, was found in 28% of patients (Table 4). The mean total cholesterol level was 204.36 mg%, mean LDL was 120.46 mg%, mean HDL was 43.61 mg%, mean TG was 165.93 mg%. Invariably all women were found to be hypercholesterolaemic. 70% of study patients were post-menopausal and only 30% were pre-menopausal with normal cycle. None of our patients were on OC pill or any hormone replacement therapy. Among menopausal women,

30 (42.2%) were diabetic as compared to 8 (26.6%) pre-menopausal women (p- 0.126374) (Table 5 & 6). In our study 44% of women who were hypertensive among them the percentage of menopausal and pre-menopausal was 42.8% and 46.6% respectively (P- 0.725071) Table 7. In our study total number of women with dyslipidaemia was 62. The incidence in premenopausal women was 33.33% as compared to menopausal women 74.28% (P- 0.00011) table 8. In our study of 100 patients, 60% of patients were diagnosed as STEMI, 28% with NSTE-UA, 12% with SIHD. (Table 9) Among STEMI group we found (n=60) 26 patients (43%) with inferior wall myocardial infarction and 34 patients (57%) with different combination of anterior wall myocardial infarction. Out of the 60% of patients with STEMI, only 20 patients (33%) were presented themselves within the window period for thrombolysis and were subsequently thrombolysed with different agents of intravenous. thrombolytics. Streptokinase, Reteplase, Tenecteplase, being used 60%, 30% and 10% of times respectively. Around 66% patients with STEMI presented beyond the window period of fibrinolysis. (Table 10 & 11) We found in our study that delayed referral from primary and secondary health centre, increased transportation time, lack of awareness being the frequent cause of delayed presentation. All patients were treated according to latest scientific guidelines. The patients with ACS were treated with antiplatelets, aspirin, statin. ACEI and beta blockers were used in pts with no contraindications. All of our patients received aspirin (100%). Clopidogrel was used in 68% patients and 32% patients received ticagrelor. (pie chart 1) The dose of clopidogrel was 300 mg loading followed by 75 mg once daily. The dose of ticagrelor was 180 mg loading followed by 90 mg twice daily. The reason for less frequent use of ticagrelor in our study was the cost and stringent condition of its use as practised in our institution. The dose of aspirin was 300 mg loading followed by 75 mg once daily in patients with clopidogrel as antiplatelet, whereas it was 75 mg once daily with ticagrelor. The angiographic distribution (refer Table 12) of CAD in women showed normal coronaries in 19% of young women and 7% of elderly women. Single vessel disease (SVD) was most frequent type of CAD (64%) in young women, whereas in elderly women TVD was most frequent (38%). (P value – 0.000081). Involvement of "left anterior descending coronary artery" (LAD) in 48.4% women, "left circumference coronary artery" (LCX) in 25.6% women, "right coronary artery" (RCA) in 26% women. (Table 13) LAD was the most common vessel involved. There was no LMCA lesion in our study group. Among the 100 patients who underwent coronary angiogram, in 78 lesions DES angioplasty, 4 lesions POBA, 12 patients were advised optimised medical treatment (OMT), 14 patients underwent CABG. 2 cases where procedure was abandoned in view of failure to cross the lesion, and they underwent CABG. The most common DES deployed was Sirolimus eluting stent (78%). Zotarolimus eluting stents were used in 10% of lesions and in 12% lesions, everolimus eluting stents were used. There were 2 incidences of coronary perforation after stent

deployment which was dealt with covered stent and they were discharged from hospital in a stable condition. 1 patient had complete heart block during the procedure, which became normal after revascularisation of RCA. Aspirin was used in all patients following procedure, and the next most common antiplatelet used was clopidogrel. High intensity atorvastatin (80 mg/day) used in all of our patients post procedure.

Age Range (yrs.)	No. of Female N= 100	Percentage (%)
35 - 44	14	14%
45 – 54	28	28%
55 - 64	26	26%
> 65	32	32%

Table 1. Age Wise Incidence of CAD in Female

Symptoms	No. of Patients n = 100	Percentage (%)
Chest pain	100	100%
SOB	12	12%
Sweating	40	40%
Vomiting	60	60%
Palpitation	34	34%

Table 2. Symptomatology

Risk Factors	No. of Female n= 100	Percentage (%)
HTN	44	44%
DM	36	36%
Dyslipidaemia	62	62%
Smoking	00	0%
Hypothyroidism	11	11%
HRT	NIL	NIL
Chemotherapy	02	2%
Family history (cad)	24	24%

Table 3. Ischemic Heart Disease Risk Factors Profile in Females

Types of Dyslipidaemia	No. of Patients n = 100	Percentage (%)
Hypercholesterolemia (>200 mg/dl)	62	62%
Hypertriglyceridemia (>150 mg/dl)	36	36%
High density lipoprotein cholesterol (<35 mg/dl)	28	28%
Low density lipoprotein cholesterol (>130 mg/dl)	42	42%

Table 4. Dyslipidaemia in female with IHD

Menstrual Status	No. of Patients n= 100	Percentage (%)
Pre-menopausal	30	30%
Menopause	70	70%

Table 5

	DM	No. DM	% of DM
Menopause	30	40	42.8%
Pre-menopause	08	22	26.6%

Table 6. Menstrual Status and Diabetes Mellitus

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	HTN	No. HTN
Menopause (n = 70)	30 (42.85%)	40 (57.15%)
Pre-menopause (n= 30)	14 (46.66%)	16 (53.34%)

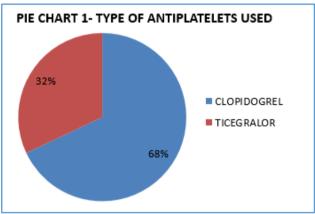**Table 7. Menstrual Status and Hypertension**

	Dyslipidaemia	No Dyslipidaemia
Menopause (n = 70)	52 (74.28%)	18 (25.72%)
Pre-Menopause (n = 30)	10 (33.33%)	20 (66.67%)

Table 8. Menstrual Status and Dyslipidaemia

Types of IHD	No. of Patients n = 100	Percentage
STEMI	60	60%
NSTE - UA	28	28%
SIHD	12	12%

Table 9. Spectrum of IHD

Fibrinolysis	No. of Patients (n = 60)	Percentage
Yes	20	33%
Delayed Presentation	40	66%

Table 10. Fibrinolysis Percentage in Patients with STEMI

Agents	No. of Patients n = 20	Percentage (%)
Streptokinase	12	60%
Reteplase	06	30%
Tenecteplase	02	10%

Table 11. Frequency Table of Fibrinolytic Agent Used

PIE CHART 1- TYPE OF ANTIPLATELETS USED
- CLOPIDOGREL 68%
- TICEGRALOR 32%

Pie Chart - 1

Parameters	Young Women (Age ≤ 50 yrs.) n = 42	Elderly Women (Age > 50 yrs.) n = 58
Normal Coronaries	08 (19.04%)	04 (7%)
SVD	27(64.28%)	20 (35%)
DVD	06 (14.28%)	12 (20%)
TVD	1(2.38%)	22 (38%)

Table 12. Angiographic Profile of Study Population

	Number (n)	Percentage (%)
LMCA	0	0%
LAD	23	48.4%
LCX	12	25.6%
RCA	12	26%

Table 13. Frequency Distribution of SVD Lesion

Abbreviations

ACEI – Angiotensin Converting Enzyme Inhibitor
ACS – Acute Coronary Syndrome
ARB – Angiotensin Receptor Blocker
AWMI – Anterior Wall Myocardial Infarction
BMS – Bare Metal Stent
CAD – Coronary Artery Disease
CAG – Coronary Angiogram
CK-MB – Creatinine Kinase- Muscle Brain
DAPT – Dual Antiplatelet Therapy
DES – Drug Eluting Stent
DM – Diabetes Mellitus
DP – Delayed Presentation
DVD – Double Vessel Disease
ECG – Electrocardiogram
ECHO – Echocardiogram
F/H – Family History
HRT – Hormone Replacement Therapy
HTN – Hypertension
IHD – Ischemic Heart Disease
IWMI – Inferior Wall Myocardial Infarction
LAD – Left Anterior Descending
LCX – Left Circumflex
LMCA – Left Main Coronary Artery
M – Menstruation
MP – Menopause
MV – Multivessel
NA – Not Applied
ND – Not Done
NSTEMI – Non-St Elevated Myocardial Infarction
OC PILL – Oral Contraceptive Pill
OMT – Optimised Medical Therapy
PCI – Percutaneous Coronary Intervention
PCOD – Polycystic Ovarian Disease
POBA – Plain Old Balloon Angioplasty
RCA – Right Coronary Artery
RT – Radiotherapy
Rt-PA – Reteplase
SIHD – Stable Ischemic Heart Disease
SK – Streptokinase
STEMI – St Elevated Myocardial Infarction
SVD – Single Vessel Disease
TIMI – Thrombolysis in Myocardial Infarction
TNK – Tenecteplase
TROP-T – Troponin- T
TVD – Triple Vessel Disease
UA – Unstable Angina
UE – Uneventful
WP – Window Period

DISCUSSION

In the present study, the demographic profile of the study population revealed the mean age to be 57 years, which is comparable to other studies conducted in India, however western studies have reported mean age higher as compared to other studies conducted in India such as study by Hochmann et al.[5] (69 years), and Chang et al.[6] (73 years).

Evaluation of the frequency of cardiovascular risk factors in the study population revealed that dyslipidaemia was the commonest risk factor (62%). The association of menstrual status with dyslipidaemia was statistically very significant in our study. (p − 0.00011) High LDL-C and high TG was the most common abnormality found in this study i.e., 40 %. Dyslipidaemia as a risk factor was higher when compared with the finding of Hochmann et al.[5] (45.5%), Chang et al.[6] (18.7%), Dave et al.[7] (58%) and Pinto et al.[8] (29%). I Shai et al.[9] observed that HDL-C related ratios were the strongest contributors to the predicting CHD and lower levels of HDL-C may be a key discriminator of higher CHD event among post-menopausal women. In my study 28% of female patients suffered from low HDL.

As there is a rise in prevalence of hypertension in female patients with CAD, 44% of women in our study were hypertensive. Similar association was observed in other studies.[10,11] The association between menstrual status and hypertension was statistically not significant in our study. P − 0.725071

The presence of diabetes was higher, i.e., 36 % to other studies like Hochmann et al.[5] (22% among both NSTEMI and STEMI), Pinto et al.[8] i.e., 24%. Even if post-menopausal females were suffering more with diabetes, the association was statistically not significant (p − 0.126374)

Chest pain was common presenting feature in 100 % of patients. SOB as the presentation was in 12% sweating in 40%, vomiting in 60% palpitation in 34%. In a study Ganeshan et al.[12] 81.8%, 28.3%, 16.2% and 9% had chest pain, SOB, syncope e, nausea and diaphoresis respectively. In another study by Chowta et al.[13] 80%, 28.3%, 13.3% 10% and 5% patients with ACS had chest pain, dyspnoea, vomiting, epigastric pain and palpitation as presenting complaints. Compared to other two studies, women from this part of the country with CAD suffer significantly more from angina, sweating, vomiting and palpitation. But the symptom of shortness of breath was relatively less in our study. None of the female patients presented with syncope in our study.

STEMI was present in 60% and NSTEMI in 28% of female patients in this study and is similar to study conducted by Parveen et al.[14] Thus in India women are more likely to have STEMI than NSTEMI which is in contrast to western population where NSTEMI is high as is observed in GRACE Registry (40% vs. 60%). Among patients with STEMI most common location of infract was AWMI (57%) followed by IW MI (43%). Jose and Gupta[15] has reported AWMI in 57%, IWMI in 39.1% and a study by Kumar et al.[16] most common type of MI in women was AWMI. But this observation was almost at par with other studies.

In this study, out of 60 female patients with STEMI 33% were given thrombolytic therapy. Large majority of patients (66 %) were not eligible for the thrombolytic therapy due to late presentation. The rate of use of thrombolytic therapy by Jose and Gupta was 82.8%. The reason for less use of thrombolytic therapy in this study was due to the relatively longer pre-hospital delay making them ineligible for the thrombolysis. Hence public awareness is found to be poor in this part of the country.

The angiographic profile of women in this study shows that normal coronaries found in 12% of women, SVD in 47% of patients, DVD in 18% of patients and TVD in 23% of women. The pattern of coronary artery involvement in this study is, LAD is the commonest (48.4%) artery involved followed by RCA (26%) and LCX (25.6%), which is as par the evidence in previous studies.[17]

CONCLUSION

Our study is a single hospital based observational study. As per our study the mean age of CAD in female in this part of India is smaller as compared to western studies. Women with CAD, from this part of the country suffer more from angina, sweating, vomiting and palpitation and less from shortness of breath. None of the patients in this study presented with syncope. Dyslipidaemia was the most common risk factor found in this study. Post-menopausal females were suffering more from dyslipidaemia as compared to women with normal cycle. (P value - 0.00011) Significant number of women have hypertension as risk factor, but the association of hypertension with menstrual status was not statistically significant. (P value − 0.725071) Post-menopausal status though was associated with more of diabetes than women with normal cycle, it was not significant statistically. More than 2/3rd of post-menopausal females were suffering from CAD as compared to pre-menopausal counterpart (1/3rd). Indian women are more likely to suffer from STEMI as compared to western counterpart. More than 2/3rd of study population with STEMI was not eligible for thrombolysis due to delayed presentation. Hence proper public awareness and awareness at PHC and CHC level can significantly improve the scenario in this part of India. Conventional risk factor management can definitely reduce the incidence of IHD and mortality related to it. The majority of women with CAD in this part are still implanted with sirolimus eluting stents as compared to western counter part, probably because of many government schemes available here.

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