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Clinical and Angiographic Profile of Suspected Coronary Artery Disease Patients in Central India

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Abstract
Introduction: *Coronary artery disease (CAD) is a leading cause of mortality worldwide and by the year 2020, will be first in the leading causes of disability. While the death rates have been declining for the past 3 decades in the west, these rates are rising in India.*
Material and Methods: *This observational study consisting of 200 subjects aimed to clarify the clinical and angiographic profile of suspected CAD patients. Following factors were analysed: age, sex, menopausal status, hypertension, diabetes mellitus, dyslipidemia, tobacco chewing, smoking, CRP, obesity, serum uric acid, family history of premature CAD, thyroid profile, USG abdomen for fatty liver and gallstones, ECG and CAG.*
Results: *The study consisted of 71% males and 29% females. Dyslipidemia (77%) was the most common risk factor followed by obesity (62%) and HTN (50%) while 32.5% were diabetics. Elevated serum uric acid (39.5%), fatty liver (20%) and gall stones (3%); subclinical (17.5%) and overt hypothyroidism (7%) were also highly prevalent. Significant correlation between independent risk factors with severity of CAD is found with Age, Diabetes mellitus, Thyroid abnormality and serum uric acid. The correlation failed to reach statistical significance between other variables.*
Conclusion: *This study confirms that along with traditional risk factors like Age, male gender,menopause, diabetes, HTN, obesity, smoking the new factors like hypothyroidism, serum uric acid, CRP, fatty liver and gallstones also play a significant role in the pathogenesis of severe CAD which if modified and treated timely can prevent the ruthless assault of severe CAD in young Indians.*
Keywords: *Angiography, CAD, CAG, CRP, Risk Factors, ECHO, ECG.*

Introduction

CAD is a leading cause of mortality worldwide[1] and by the year 2020, will be first in the leading causes of disability.[2] Projections show that CAD has reached epidemic proportions in many developing countries. While the death rates have been declining for the past 3 decades in the west, these rates are rising in India. In India, mortality attributable to CAD has risen by 103% in men and by 90% in women from 1985 to 2015.[3] More importantly, CAD tends to occur at a younger age in Indians, with more extensive involvement[4] contributed by genetic, metabolic, conventional and nonconventional risk factors.[5,6]

Of particular concern to India is not only the high burden of cardiovascular diseases (CVDs), but also the effects of these diseases on the productive workforce aged 35–65 years. Heart diseases are rising in Asian Indians 5 –10 years earlier than in other populations around the world.[7] The mean

age for first presentation of acute myocardial infarction in Indians is 53years.[8] Coronary artery disease (CAD) that manifests at a younger age can have devastating consequences for an individual, the family, and society. Therefore, to stop the ruthless assault of CAD in developing countries, there is an urgent need to study the clinical profile of patients presenting with Acute Coronary Syndrome and correlation of various risk factors with the angiographic findings. The main aim of this study is to evaluate the clinical profile, risk factor profile and correlate various risk factors with the angiographic profile of individuals with suspected CAD.

Materials and Methods

Total 200 patients who were suspected to have coronary artery disease and were admitted to Department of Medicine and Cardiology, Gandhi Medical College & Hamidia Hospital between 1-04-2015 to 31-5-2016 were included in this study. Patients either unwilling or unsuitable for CAG will be excluded.

Their clinical profile and risk factor profile were studied and their effects on angiographic profile were analysed.

The following data were included for analysis:

- Age
- Sex
- Menopausal status
- HYPERTENSION: systolic blood pressure ≥140 and/or diastolic ≥90 mmHg and/or on anti-hypertensive treatment
- DIABETES MELLITUS: symptoms of diabetes and plasma glucose concentration ≥200 mg/dl (11.1 mmol/L), or fasting blood sugar ≥126 mg/dl (7.0 mmol/L)
- ADDICTION: Cigarette/ bidi smoking/ tobacco chewing history (patients who were actively consuming tobacco/bidi or had quit within last 2 months were considered as substance abuser and patients who had quit beyond 2 months were considered in the category of no addiction)
- DYSLIPIDEMIA was defined as the presence of any of the following:
- Total cholesterol >200 mg/dl, triglycerides (TG) >150 mg/dl, low-density lipoprotein (LDL) >130 mg/dl, and high-density lipoproteins (HDL) <50 mg/dl in females and <40 in males.
- FAMILY HISTORY OF CAD: first degree relatives before the age of 55 years in men and 65 years in women.
- C-reactive protein status post MI.
- Fatty liver, gallstones: identified on USG
- HYPOTHYROIDISM: Patients were defined as having subclinical hypothyroidism when TSH >5.5 micro international units/ml with normal values of T3 & T4, and as overt hypothyroidism if they were having low values of T3 & T4 or were taking tab thyroxine.
- OBESITY was defined using the waist hip ratio where a ratio > 0.85 in women and >0.95 in men.
- Echocardiography (Left ventricular ejection fraction)
- Coronary angiography results

Clinical manifestations, left ventricular ejection fraction, coronary angiographic findings and type of infarction as assessed by ECG were reported. Selective coronary angiogram was done using standard technique unless patient was hemodynamically unstable or with deranged renal parameters. Significant/Obstructive CAD was defined as a diameter stenosis >70% in each major epicardial artery (or any of its major branches-diagonal, obtuse marginal, ramus intermedius, posterior descending artery, and posterolateral branch) except left main disease where a stenosis of > 50% was considered significant. Patients were classified as having single-vessel disease (SVD), double-vessel disease (DVD) or triple vessel disease (TVD) accordingly. Normal vessels were defined as the complete absence/ <20% stenosis in the left main coronary artery (LMCA), left anterior descending (LAD), right coronary artery (RCA), and left circumflex (LCx) as well as

in their main branches (diagonal, obtuse marginal, ramus intermedius, posterior descending artery, and posterolateral branch). For comparative analysis patients were categorised into two groups based on their cardiac catheterization findings (i.e. angiographic non obstructive cases who did not have significant stenosis in any of the coronary artery and obstructive CAD who had significant stenosis in atleast one coronary artery). Severe CAD is defined as multivessel involvement (DVD/ TVD and /or LMCA). The risk factors included in the study were analysed and their impact on angiographic findings. The pattern of CAD as assessed by CAG was correlated with various risk factors.

Statistical Analysis

Data was expressed as Mean ± S.D. and Percentage. Linearity of data was assessed using Kolmogorove-smirnov analysis. Chi-square test was used to assess the significance of difference between frequency distribution and association of various risk factors with Severity of CVD. ANOVA followed by post hoc Tukey's HSD test was used to compare mean between more than two study groups. Multiple regression analysis was used to assess the individual risk assigned by each risk factor for severity of CVD. Statistical calculations were done using SPSS Vs 16 ®, (IBM™ Corp Pvt. Ltd).

Result

In our study most of the patients who were suspected to have CAD and underwent CAG were in the age group of 41-50years (32%). Age and gender profile is shown in table 1. The mean age of patients in our study having non obstructive CAD on CAG was 48.23 ± 8.97, SVD was 48.9 ± 10.24, DVD was 58.10 ± 7.6, TVD was 52.45 ± 10.44 and those with involvement of left main was 55.09 ±10.25. Further, it was noted that non obstructive CAD on angiography was more common in females (7.5% Vs 5.5%) while frequency of single vessel disease (34% Vs 7.5%), double vessel disease (11.5% Vs 5%), triple vessel disease (13.5% Vs 5%) and involvement of LMCA (6.5% Vs 4%) was higher in males. Out of total 58 female, majority i.e. 43 (74.13%) were postmenopausal while remaining 15 (25.86%) were premenopausal and postmenopausal women had more frequency of severe obstructive CAD i.e. SVD (6% Vs 1.5%), DVD (5% Vs 0%), TVD (3% Vs 1.5%) and LMCA (2.5% Vs 1.5%) than premenopausal women. Dyslipidemia is the most common risk factor associated with CAD in our study.77% (154 out of 200) patients had dyslipidemia as per the criteria. Although elevated LDL was the most common form of dyslipidemia occurring in 66.55% of study subjects followed by elevated triglycerides (54.5%), the predominant form of dyslipidemia was elevated triglycerides with mean value of 157.47± 89.4 mg/dl. The second most common risk factor was obesity in our study being present in 62% of study subjects based on the waist hip ratio (>0.85 in females and > 0.95 in males). All the more, we found that the frequency of non obese patients is more with non obstructive CAD (7.5% Vs 5.5%) as compared to obese patients. In our study, 50% of subjects were hypertensive. Frequency of non obstructive CAD (9% Vs 4%) and single vessel disease (25% Vs 16.5%) were found to be higher in normotensive subjects while hypertensive subjects showed higher frequency of double vessel disease (10% Vs 6.5%), triple vessel disease (12.5% Vs 6%) and involvement of LMCA (7% Vs 3.5%). Diabetes was found in 32.5% of patients with CAD in our study. Frequency of non obstructive CAD on coronary angiography was found to be higher in non diabetic subjects than diabetics (11%Vs 2%). Same findings were observed regarding frequency of single vessel disease (33% Vs 8.5%) and double vessel disease (12% Vs 4.5%) while frequency of triple vessel disease was found to be significantly higher in diabetics (12.5% Vs 6%). 30% of the study subjects had family history of CAD. We found that 23% of our study subjects were addicted to either bidi or cigarette smoking. High frequency of non smokers were noted among patients with non obstructive CAD in coronary angiography, further the

frequency of smokers was found to be consistently increasing in subjects with SVD (6% Vs 35.5%), DVD (6.5% Vs 10%) and TVD (8% Vs 10.5%). Our study subjects consisted of 17.5% of tobacco chewers. Although most of the patients had normal USG findings (73.5%), there was a high frequency of fatty liver (20%) in CAD patients of central India. Gallstones and altered echotexture of renal parenchyma were found in 3% each of study subjects. While most of the study subjects had normal thyroid profile (70.5%), a high frequency of subclinical hypothyroidism (17 %) and overt hypothyroidism (7%) was found in CAD patients of central India. Also, increasingly higher frequency of subclinical hypothyroidism is noted with increasing severity of CAD i.e. SVD (4%), DVD (3.5%), TVD (5.5%) and LMCA (3.5%). Same was the observation with overt hypothyroidism (TVD- 5%, DVD-0%, SVD-0.5% and LMCA- 1.5%)[p<0.0001]. Elevated serum uric acid (39.5%) was a very common risk factor in patients with CAD. There was a high frequency of patients with normal serum uric acid in Non obstructive CAD (9.55 Vs 3.5%), SVD (30% Vs 11.5%) and DVD (10% Vs 6.5%) while the frequency of subjects with elevated serum uric acid increased considerably in TVD (11.5% Vs 7%) and LMCA involvement (6.5% Vs 4%)[p=0.001]. In our study 41% of study subjects had positive CRP.As the severity of CAD increased the frequency of subjects with negative CRP decreased (p<0.0001).

Multiple regression analysis was performed for independent association of various risk factors with severity of CAD as assessed on angiography. Significant independent risk for severity of CAD as suggested by significant correlation was found with Age (p=0.001), Diabetes mellitus (p<0.0001), Thyroid abnormality (p=0.001) and uric acid (p=0.02). The correlation failed to reach statistical significance between other variables

Table 1. Age and gender distribution of study subjects

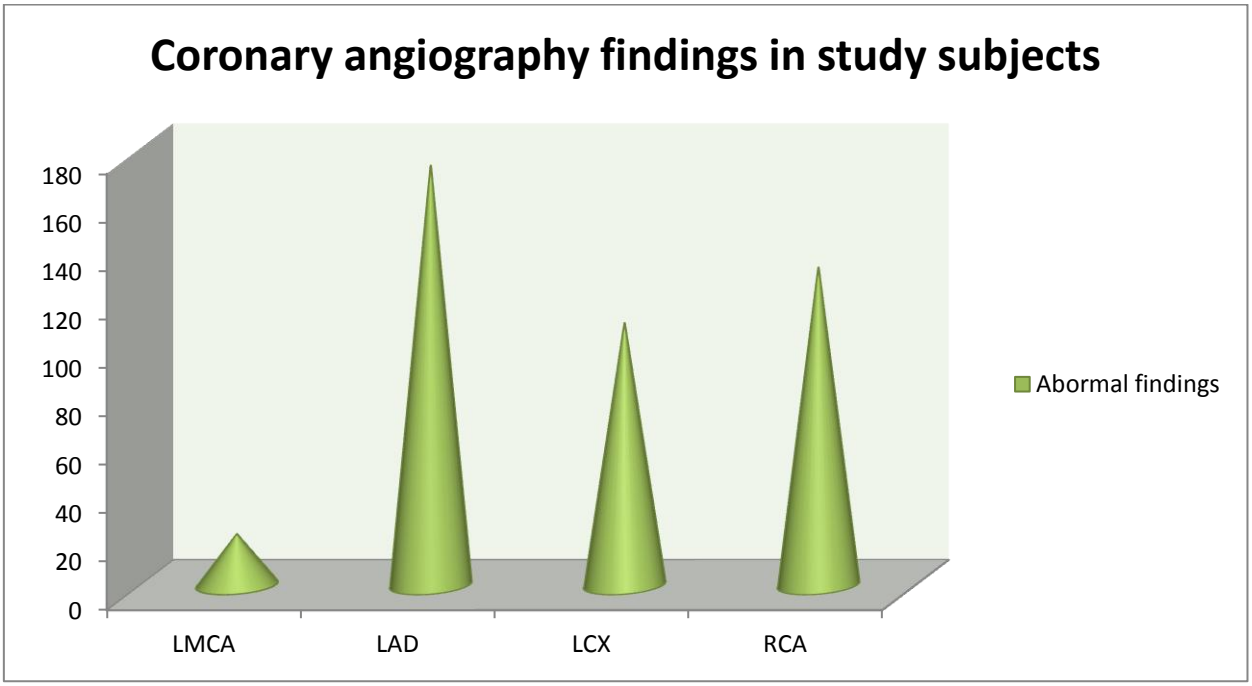
Age groups		Gender		Total
		Female	Male	
≤30	Count	0	4	4
	% of Total	.0%	2.0%	2.0%
31-40	Count	11	23	34
	% of Total	5.5%	11.5%	17.0%
41-50	Count	13	51	64
	% of Total	6.5%	25.5%	32.0%
51-60	Count	21	39	60
	% of Total	10.5%	19.5%	30.0%
61-70	Count	13	24	37
	% of Total	6.5%	12.0%	18.5%
>70	Count	0	1	1
	% of Total	.0%	.5%	.5%
Total	Count	58	142	200
	% of Total	29.0%	71.0%	100.0%

Table 2: Pattern of Coronary angiographic Findings in study subjects

Coronary angiography findings	No. Of subjects	Percentage
Normal/Insignificant CAD	26	13
SVD	83	41.5
DVD	33	16.5
TVD	37	18.5
LMCA involvement	21	10.5

Table3: Risk Factors For Coronary Artery disease in Study subjects.

Cardiovascular risk factor	No. of subjects	Percentage
Dyslipidemia	154	77
Hypertension	100	50
Diabetes mellitus	65	32.5
Smoking	46	23
Tobacco	35	17.5
Obesity	124	62
Family history	60	30



Correlation of various risk factors with severity of CAD as found on angiography by multiple regression analysis.

Coefficients[a]						
		Unstandardized Coefficients		Standardized Coefficients		
Model		B	Std. Error	Beta	t	Sig.
1	(Constant)	-.989	.460		-2.150	.033
	Age (years)	.029	.009	.248	3.351	.001
	Gender	.146	.170	.055	.856	.393
	Hypertension	.237	.155	.098	1.529	.128
	Diabetes Mellitus	.682	.165	.264	4.141	.000
	Smoking	.297	.191	.103	1.555	.122
	Tobacco Chewing	-.133	.196	-.042	-.681	.497
	Dyslipidemia	.164	.177	.057	.928	.355
	Obesity	.132	.164	.053	.803	.423
	Family history	.278	.170	.105	1.632	.104
	Thyroid status	.225	.070	.205	3.232	.001
	Uric acid	.381	.162	.154	2.356	.020
	CRP	.333	.169	.135	1.968	.051
Dependent Variable: CAD Severity						

Discussion

There has been an explosive increase in the knowledge of CAD in west in the past decade. Most of the studies in India correlated the various risk factors with prevalence of CAD. There is not much published data on predictors of angiographic severity of CAD in India. It was decided to undertake this study to fill in the gap with little knowledge on the profile and pattern of CAD in people residing in central India.

Majority of patients with CAD in our study are young males belonging to age group 41-50 years. As age increased, the severity of CAD increased with significant difference between non obstructive CAD and DVD; and SVD and DVD groups ($p<0.05$ for both). CAD in males occurs at an earlier age than females and men have significantly ($p=0.003$) more frequency of multi vessel disease than women. Menopause is found to be significantly ($p=0.002$) associated with increased severity of CAD. Gupta and Ghaffar et al.[9,10] reported that western countries where CAD is considered a disease of the aged, 23 percent of CAD deaths occur below the age of 70; compared to 52 percent of CAD deaths occurring among people under 70 years of age in India. Our finding was consistent with Gupta et al[11] who reported in their study that the mean age of presentation was higher in females (64.36±8.82 years) as compared to males (57.28±11.30 years). Young women with CAD comprise an especially interesting group given the protective effect of estrogen, but which factors are predictive in this distinctly unusual cohort is poorly understood[12]. Dyslipidemia is the most common risk factor associated with CAD in Central India followed by obesity and hypertension with all three of them significantly ($p=0.004$, $p=0.001$and $p=0.003$ respectively) associated with increased severity of CAD. Most of the patients with diabetes are young and have significantly ($p=0.0001$) more frequency of triple vessel disease. Haastrupet al showed that 83% of patients admitted for CAG for suspected CAD suffered from previously or presently recognized dyslipidemia and 74% were dyslipidemic at admission[13]. Although elevated LDL was the most frequent form of dyslipidemia in our study, occurring in 66.55% of study subjects followed by elevated triglycerides (54.5%), the predominant form of dyslipidemia was elevated triglycerides with mean value of 157.47± 89.4 mg/dl. A low HDL was found in 47.5% of patients and high total cholesterol in 44% of study subjects. Rafaela et al.[14] in their study on lipid profile and severity of atherosclerotic disease in ACS after analysis of LDL showed that this variable increased with the number of vessels affected. Gupta et al.[11]found that the prevalence of obesity using waist hip ratio as the criteria was 33.8% which is less than the prevalence seen in south asian cohort of INTERHEART study (44.2%). Laurent Larifla et al.[15] found that obese patients with CAD less frequently had multivessel lesions, so obesity appeared to be an independent protective factor against severe CAD in Afro-Caribbean patients

Mahadeva Swamy BC et al.[16] concluded that statistically significant positive correlation between duration of diabetes and Gensini scores (P value 0.007). No significant association is noted between family history and severity of CAD ($p=0.12$). Amvita banerjee et al.[17] in their study concluded that sex-specific family history data do not predict angiographic localization of coronary disease in patients presenting with ACS. Smoking is found to be significantly associated with severe CAD ($p<0.0001$) and is very common in males in central India. Association between tobacco chewing and severity of CAD failed to reach statistical significance ($p=0.141$).

There is a considerably high frequency of fatty liver (20% of study subjects) on USG abdomen in patients with CAD and is significantly ($p=0.0001$) associated with multi vessel CAD. Similar association has been found in patients with gallstones and altered echotexture of renal parenchyma with severity of CAD. Alper AT et al.[18] found that patients with NAFLD had significantly higher body mass index, waist circumference, and serum triglyceride level, and significantly lower HDL-cholesterol level

(p<0.001). While most of the study subjects had normal thyroid profile (70.5%), a high frequency of subclinical hypothyroidism (17 %) and overt hypothyroidism (7%) was found in CAD patients of central India and suggests that hypothyroidism plays a significant role in pathogenesis of severe CAD (p<0.0001). Xue Chao et al.[19] showed that the low T3 syndrome is most common thyroid dysfunction in patients with coronary heart disease, and patients with low FT3 are more likely to multi-vessel involvement. A raised serum uric acid is also significantly (p=0.001) associated with increased frequency of TVD and LMCA involvement. Thus, it is a very important risk factor which if treated early, even when not associated with symptoms of gout can help reduce the risk of severe CAD. Duran M et al.[20] reported that patients with hyperuricemia had higher Gensini score, high number of diseased vessels, critical lesions, and total occlusion. Patients with a positive CRP had significantly more frequency of multi vessel disease (p< 0.0001).The major limitation of our study was that we could not use hsCRP which is more sensitive. Syed Shahid Habib et al[.21] found that hsCRP is a marker of the presence and severity of CAD defined by Gensini scoring or vessel scoring. Most of the patients in our study had SVD (41.5%) followed by TVD (18.5%), DVD (16.5%) and Non obstructive CAD (normal/ insignificant CAD) in 13%. LMCA was involved in 10.5% of our study subjects. Amongst individual vessels, the most common vessel affected by atherosclerosis is LAD (86.5%) followed by RCA (65.5%). LCx was diseased in 54 % patients.

Significant independent risk for severity of CAD as suggested by significant correlation is found with Age (p=0.001), Diabetes mellitus (p<0.0001), Thyroid abnormality (p=0.001) and serum uric acid (p=0.02). The correlation failed to reach statistical significance between other variables.

Moderately strong uphill correlation (R=0.638) is noted between presence of multiple risk factors [CRP, Age (years), Gender, Tobacco Chewing, Serum Uric acid, Dyslipidemia, Diabetes Mellitus, Thyroid Abnormality, Hypertension, Family history, Obesity, Smoking] and severity of CAD.

The study limitations include the non inclusion of factors like

- hsCRP,
- free T3 levels,
- Scoring system for CAD severity like the Gensini score.

Conclusion

This study confirms that along with traditional risk factors like age, gender, menopause, obesity, dyslipidemia, smoking, diabetes and HTN; novel risk factors like hypothyroidism, fatty liver, gallstones, serum uric acid and CRP also play significant role in the pathogenesis of severe CAD which if detected timely, and modified accordingly, can help in preventing the ruthless assault of severe CAD in young Indians.

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