



High Sensitive C- Reactive Protein in Patients with Angiographically Proved Coronary Artery Disease

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Introduction: Atherosclerosis is associated with increased inflammatory activity and risk of vascular disease. The hypothesis is that, the hs-CRP testing might have prognostic usefulness for patients with CAD. Considering a major role of hs-CRP in atherothrombosis, its measurements can provide a novel method to detect individuals at high risk of rupture of plaque.

Aim of the Work: This study was performed to find out the relation of high sensitive CRP (hs-CRP) with angiographically proved coronary artery disease (CAD) and its severity.

Methodology: Total 125 patients underwent CAG in present study, of them 36% were females and 64% were males, predominated by male sex ('p' <0.001).

Results: The mean for hs-CRP levels was 1.67(±0.85) mg/L and significantly high in patient with CAD. Strong correlation was formed between age ≥ 45 years and hs-CRP 1-3 mg/ L in present cohort of CAD. About one third of population with CAD had dyslipidemia of them majority (2/3rd) had hs-CRP 1-3 mg/L. Two-third of patients with CAD with tobacco consumption in any form had hs-CRP 1-3 mg/L and was significant than < 1 mg/L and >3 mg/L hs-CRP level. The hs-CRP level associated favorably with the frequency and extent of the CAD in present study (r=0.664).

Conclusion: High sensitive CRP offers better risk stratification, predictive and prognostic value, in patients with CAD. Further studies and interventions are mandatory to identify the independent role of hs-CRP as a CAD risk factor and its cost effectiveness in a population of a developing country like India.

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1. INTRODUCTION

India faces the highest global risk of coronary artery disease (CAD). The major modifiable risk factors for CAD include hypertension (HTN), diabetes mellitus (DM), smoking, and hyperlipidemia, while non-modifiable risk factors include premature CAD, age, gender and family history. Atherosclerosis is associated with increased inflammatory activity and risk of vascular disease. The hypothesis is that, the hs-CRP testing might have prognostic usefulness for patients with CAD. Considering a major role of hs-CRP in atherothrombosis, its measurements can provide a novel method to detect individuals at high risk of rupture of plaque [1]. Nevertheless, extensive data has been obtained from western studies [2-4]. So far there is scanty and paucity of data from India. Considering the increasing incidence and severity of coronary atherosclerosis it is importance to know about hs-CRP as a marker of atherothrombosis. The present study was conducted to determine the relation between serum hs-CRP levels and severity of coronary atherosclerosis in a Cohort of CAD in tertiary care teaching hospital.

1.1 Aim and Objectives

1.1.1 Aim

To find out relation of high sensitive CRP (hs-CRP) with angiographically proved coronary artery disease (CAD) and its severity.

1.1.2 Objectives

To study conventional/traditional coronary artery disease risk factor. To study the clinical, biochemical and angiogram profile of patients with coronary artery disease. To study hs-CRP level in patients undergoing coronary angiogram. Relation of hs-CRP to metabolic syndrome (MeTS).

2. REVIEW OF LITERATURE

Worldwide, cardiovascular atherosclerotic disorder and coronary artery disease is considered the leading cause of mortality and reduction of disability-adjusted life years. Significant short-term inter-individual variation in hs-CRP levels appeared as a recent examination of a subset of the National Health and Nutrition Examination Survey (NHANES) database. The

use of single hs-CRP measures to risk stratify patients can misclassify a large number of individuals. Accelerated atherosclerosis disease involving metabolic syndrome, obesity, and insulin tolerance are correlated with elevated hs-CRP rates. In comparison to cells in atherosclerotic plaques, adipose tissue is a significant source of IL-6, which may clarify the strong relationship between hs-CRP and obesity. An appropriate dose of hs-CRP to identify increased risk of CV: Research from large-scale clinical studies has used a 2 mg/L hs-CRP break point to describe increased risk of CV.

Y. Kamath [5] studied The role of low-grade systemic inflammation as evidenced by high-sensitivity rates of C-reactive protein (hs-CRP) in the pathogenesis of atherosclerotic vascular disease has been extensively studied in empirical studies and clinical trials over the last two decades. Hs-CRP measurement was integrated into the Reynolds risk scoring system to predict cardiovascular risk, based on evidence that has accrued.

Ridker PM. [6] conducted that prospective results also suggest that CRP is a better indicator of mortality than low-density lipoprotein (LDL) cholesterol. In the largest analysis to date, both the region under the receptor operator characteristic (ROC) curve (0.64 vs. 0.60) and the population at risk rate (40 vs. 19) is slightly higher for CRP than for LDL cholesterol.

Shen J, Ordovas JM [7] studied that inflammation assumes an important function at all levels of atherosclerosis. High-sensitivity C-reactive protein (hs-CRP), a systemic inflammatory precursor, has earned acceptance as an important risk factor for cardiovascular disease (CVD).

3. MATERIALS AND METHODS

This prospective observational study and was conducted over 18 month duration from October 2014 to March 2016. The patients undergoing coronary angiogram for evaluation of CAD of both genders at Krishna Institute of Medical Sciences Karad, were included in this study.

4. OBSERVATION AND RESULTS

Total 125 patients fulfilling inclusion criteria were included in current prospective non-interventional observational study, conducted on

patient with coronary artery disease CAD) undergoing coronary angiogram. Total 80 (64%) male and 45 (36%) female patients undergoing coronary angiogram were included in present study after informed and written consent as per protocol.

The mean for age was 58.22 (\pm 11.47), the mean for serum Cholesterol was 192.65 (\pm 29.29), for serum Triglyceride was 135.42 (\pm 38.67), for HDL was 45.03 (\pm 10.41), for LDL was 115.21 (\pm 21.45). The mean for BSL (F) was 147.74 (\pm 37.53), for hs-CRP was 1.67 (\pm 0.85), for systolic BP (SBP) was 142.56 (\pm 13.37), for diastolic BP (DBP) was 85.86 (\pm 7.44) and for waist circumference was 102(\pm 13.7) [Table 1].

High sensitive CRP was positively correlated with severity of coronary artery disease (Pearson $r=0.6648$), weak positive correlation with blood sugar level, systolic and diastolic blood pressure and weak negative correlation with components of lipid profile [Table 2].

Of total 27 patients with normal CAG, 11(40.70%) were males, 16 (59.25%) were females. Total of 42 patients with SVD,

32(76.19%) patients were Males, 10(23.81%) were Females. Total of 26 patients with DVD, 19(73.08%) were Males, 7(26.92%) were females. Total of 30 patients with TVD, 18(60.00%) were Males, 12 (40.00%) were females. [Table 3] SVD and DVD were more prevalent in male population ($p < 0.03$) and TVD and normal CAG was observed in female population ($p < 0.02$) [Table 3].

Total of 42 patients with SVD, 24 (57.14%) were farmers by occupation, 5 (11.90%) were shopkeeper, 1(2.38%) was plumber, 8 (19.05%) were housewives, 5 (11.90%) had business of their own. Total of 26 patients with DVD, 19 (73.08%) were farmers 3 (11.54%) were shopkeepers, 4 (15.38%) were housewives, 2 (7.69%) had business of their own. Total of 30 patients with TVD, 24(80%) were farmers, 1(6.67%) was a plumber, 4 (13.33%) were housewives. Of total 27 patients with normal CAG, 13 (48.14%) were farmers, 6 (22.2%) were shopkeepers, 2(7.40%) were workers, 9 (33.3%) were housewives. [Table 4] The severity and prevalence of CAD was more in farmers compared to other occupation in present cohort of patients with CAD ($p < 0.002$) [Table 4].

Table 1. Mean and standard deviation of various CAD risk factors

CAD risk factors	Mean	SD (\pm)
1. Age	58.22	11.47
2. Serum Cholesterol (mg/dl)	192.65	29.29
3. Serum Triglycerides (mg/dl)	135.42	38.67
4. HDL cholesterol (mg/dl)	45.03	10.41
5. LDL cholesterol (mg/dl)	115.21	21.45
6. Blood sugar level (F) (mg/dl)	147.74	37.53
7. hs-CRP (mg/L)	1.67	0.85
8. Systolic blood pressure (SBP) mmHg.	142.56	13.37
9. Diastolic blood pressure (DBP) mmHg.	85.68	7.44
10. Waist circumference (WC) cm.	102	13.7

Table 2. Correlation of hs-CRP levels with CAD risk factors and severity of CAD

Variables of CAD	hs-CRP :	Correlation (r)
CAD (SVD,DVD, TVD)		0.664849289
DBP		0.179334387
SBP		.14433076
BSL		0.007327962
HDL		-0.002560712
LDL		-0.12779243
T-CHO		-0.169474801
TRG		-0.076220922

Table 3. Demographic distribution of coronary angiographic vessel involved

	Male	%	Female	%
SVD (n=42)	32	76.19	10	23.81
DVD (n=26)	19	73.08	7	26.92
TVD (n=30)	18	60.00	12	40.00
Normal CAG (n=27)	11	40.70	16	59.25

Table 4. Relation of occupation to CAD and their anatomy and severity

	Farmer (%)		Shopkeeper (%)		Worker (%)		Housewife (%)		Business (%)	
SVD (n =42)	24	57.14	5	11.90	1	2.38	8	19.05	5	11.9
DVD (n=26)	19	73.08	3	11.54	0	0.00	4	15.38	2	7.69
TVD (n=30)	24	80	0	0	2	6.67	4	13.33	0	0
N-CAG (n=27)	13	48.14	6	22.2	2	7.40	9	33.3	0	0

Table 5. Prevalence of addiction according to vessel affected

Risk factors	SVD (n =42)	DVD (n=26)	TVD (n=30)	N (n=27)
Tobacco (Total)	25 (57.14%)	13 (50%)	13 (43.33%)	9 (33.3%)
Tobacco (M)	23 (54.76%)	12 (46.15%)	1 (3.33%)	8 (29.62%)
Tobacco (F)	2 (4.76%)	1 (3.84%)	12 (40%)	1 (3.70%)
Alcohol	12 (28.57%)	6 (23.07%)	6 (20%)	3 (11.1%)
Mishri (Total)	9 (21.42%)	9 (34.61%)	15 (50%)	9 (33.3%)
Mishri (M)	1 (2.38%)	3 (11.53%)	4 (13.33%)	2 (7.40%)
Mishri (F)	8 (19.04%)	6 (23.07%)	11 (36.66%)	7 (25.92%)
Smoking (Total)	5 (11.90%)	2 (7.69%)	2 (6.66%)	2 (7.40%)

Of total 50 patients who consumed tobacco, 25 (57.14%) patients had SVD, 13(50%) patients had DVD, and 13 (43.33%) patients had TVD. Total of 36 male patients who consumed tobacco, 23 (54.76%) had SVD, 12(46.15%) had DVD, 1(3.33%) had TVD. Total of 15 female patients who consumed tobacco, 2(4.76%) had SVD, 1(3.84%) had DVD, 12(40%) had TVD. Total of 24 patients who consumed alcohol 12(28.57%) had SVD, 6(23.07%) had DVD, 6(20%) had TVD. Total of 33 patients who used misery, 9 (21.42%) had SVD, 9 (34.61%) had DVD, 15(50%) had TVD. Total of 8 male patients who used mishri, 1 (2.38%) had SVD, 3(11.53%) had DVD, 4(13.33%) had TVD. Total of 25 female patients who used misery, 8(19.04%) had SVD, 6(23.07%) had DVD, 11(36.66%) had TVD. Total of 9 patients who smoked cigarettes, 5(11.90%) had SVD, 2(7.69%) had DVD, 2(6.66%) had TVD. Tobacco consumption in any form was significantly associated with SVD and DVD than TVD or normal CAG with IHD [Table 5].

5. DISCUSSION

Total 111 (88.8%) patients were aged ≥ 45 years. Age ≥ 45 years, male gender, low HDL cholesterol and high LDL cholesterol were the most prevalent CAD risk factor in present cohort of CAD. In present study about one third of population with CAD had dyslipidemia of them majority (2/3rd) had hs-CRP 1-3 mg/L. Two-third of patients with CAD with tobacco consumption in any form had hs-CRP 1-3 mg/L and was significant than < 1 mg/L and > 3 mg/L hs-CRP level. Total 125 patients underwent CAG in present study, of them 80 (64%) male and 45 (36%) female patients predominated by male gender ('p' < 0.001). In present study single vessel disease (SVD) on coronary angiogram was more prevalent compared to DVD and TVD. Total 80 (72.07%) patients had hs-CRP ranging 1-3 mg/L. The hs-CRP between 1-3 mg/L had better predictive value in SVD and for DVD while hs-CRP > 3 mg/L, had predictive value for TVD. SVD was common in < 45 years and DVD and TVD were common in ≥ 45 years patients ('p' $<$

0.05). The hs-CRP level was positively correlated with severity and extent of CAD in present study ($r=0.47$).

In our study 2/3rd of patients with CAD with tobacco consumption in any form had hs-CRP 1-3 mg/L. In multivariate analysis in present study after controlling age there was strong association between age ≥ 45 years, dyslipidemia (2/3rd), smoking and hs-CRP level 1-3 mg/L ($p < 0.02$). The hs-CRP level was positively correlated with severity and extent of CAD in present study ($r=0.664$). Razban M. M. et al reported no significant correlation between serum levels of hs-CRP and severity and angiographic extent on coronary arteries [8]. This could be because of various reasons like sample size, inclusion exclusion criteria. Present cohort of CAD undergoing CAG comprises 64% male and 36% female patients predominated by male gender ($p < 0.001$) with mean for hs-CRP levels was 1.67 (± 0.85) of them about 2/3rd patients had hs-CRP ranging between 1-3 mg/L. The hs-CRP level was positively correlated with severity and extent of CAD in present study.

6. CONCLUSIONS

We found that elevated high sensitive C reactive protein was a strong predictor of coronary artery disease with positive correlation, after adjustment for baseline characteristics like, age, gender, tobacco, dyslipidemia. Significant CAD by Coronary angiogram (CAG) was apparent in patients with hs-CRP of 1 to 3 mg/L. Present study observations suggest that among patients with coronary artery disease, hs-CRP levels can be used to predict, which patients can have significant CAD and consequently requiring intervention. High sensitive CRP offers better risk stratification, predictive and prognostic value, in patients with CAD. Currently there is no mandate to measure hs-CRP in all patients with coronary artery disease. Ongoing trials will elucidate and clarify the benefit of targeting drug therapy for CRP levels. There is a positive correlation with serum HS-CRP levels and disease burden in the inflammatory CAD patient. Further studies and interventions are mandatory to identify the independent role of hs-CRP as a CAD risk factor and its cost effectiveness in a population of a developing country like India.

CONSENT

As per international standard or university standard, patients' written consent has been collected and preserved by the authors.

ETHICAL APPROVAL

Present study was approved by Ethics and protocol committee KIMSDU Karad.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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