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Biochemistry

ROLE OF HS CRP AND LIPID ABNORMALITIES AS RISK FACTOR IN CORONARY ARTERY DISEASE

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ABSTRACT

BACKGROUND: In recent years, data suggesting that certain markers of inflammation play a key role in the development and progression of atherosclerosis. hsCRP has shown promising results as a predictor of Coronary Artery Disease(CAD).

OBJECTIVES: To evaluate the significance of CRP as one of the most reliable markers in coronary artery disease and to study the role of lipid abnormalities as a risk factor in coronary artery disease.

MATERIALS AND METHODS: Study was conducted at MedicalCollege, Kolkata.30 cases and 30 controls were studied. Angiographically proven cases of CAD aged between 40- 60 years of both sexes were included in the study as cases. Age and sex matched individuals without CAD weSre considered as cases. Patients with recent myocardial infarction, unstable angina (<6months).and with other inflammatory conditions were excluded from the study.

RESULTS: hsCRP was significantly higher in CAD cases2.0±1.4 compared with controls0.8±0.7 and this was statistically significant <0.001.Lipid parameters such as Total Cholesteol,Triglycerides and Low density lipoprotein were elevated in cases compared with controls and was found to be statistically significant. Blood glucose parameters both in fasting and post-prandial conditions were found to be elevated in cases compared with controls.

CONCLUSION: The study thus suggests that hsCRP level appears to be a dependable marker of CAD.Thus, hsCRP can be used as a sensitive predictor of CAD.

KEYWORDS : hs CRP,Coronary Artery Disease

INTRODUCTION

Coronary artery disease is one of the major health problems worldwide and in India in particular. WHO has declared coronary artery disease as "Modern Epidemic".

Risk factors have traditionally been used to define the statistical likelihood of the development of clinical coronary disease in populations of asymptomatic patients.[1]

Nowadays, the atherosclerotic process and its complications are recognized as the main culprit of coronary heart disease morbidity and mortality. To date, many risk factors for atherosclerosis development, progression and complications have been identified in clinical, experimental and population based studies (such as hypertension, diabetes, hypercholesterolaemia, cigarette smoking etc). These are known as "traditional risk factors".[2]

During the last few years a growing body of evidence has demonstrated that inflammation plays a pivotal role in the pathogenesis of atherosclerosis and its complications, and nowadays atherosclerosis is considered as an "inflammatory disease". Accumulating data demonstrate that elevated levels of circulating inflammatory markers predict an unfavourable cardiovascular outcome in asymptomatic subjects, (patients with stable ischaemic heart disease and in patients with acute coronary syndromes). Improved knowledge of the molecular and cellular mechanisms of inflammation might not only further improve prognostic stratification but also allow us to identify novel therapeutic targets.[3]

Several acute phase reactants, cytokines, and soluble cellular adhesion molecules have been implicated in this process, with their plasma concentrations increased in variety of atherosclerotic diseases.

Several prospective studies have shown that CRP is a predictor of increased risk of MI, stroke or peripheral vascular disease in asymptomatic individuals with no known coronary heart disease.[4]

High sensitive C-reactive protein (and not conventional CRP) is believed to be in the absence of other contributing factors as one of the best predictors of cardiovascular

In addition to the lipid profile, an assessment of CRP dramatically improves the risk prediction of coronary artery disease. A few studies have indicated negative correlation between CRP and high-density lipoprotein cholesterol. A comparison of changes in CRP to the altered lipid parameters is also attempted in the study. Thus an attempt is made to highlight how the different predictors of cardiovascular disease compare with each other.

In this background, a study was done to assess the role of CRP and lipid abnormalities as risk factors in coronary artery disease**.**

MATERIALSANDMETHODS:

This is a Hospital based case control study which was undertaken in Medical College-Kolkata after obtaining ethical clearance from the institution. Angiographically proven cases of CAD aged between 40-60 years of both sexes were included in the study as cases. Age and sex matched individuals without CAD were considered as cases. Patients with recent myocardial infarction, unstable angina (<6months).and with other inflammatory conditions were excluded from the study.Pre-structured, pre-tested proforma was used for data collection.hsCRP (by Immunonephelometry),Lipid parameter,Blood urea, serum creatinine, urine albumin were measured. LDL and VLDL calculation by Friedewald's equation.

STATISTICALANALYSIS:

Was done using SPSS package. Student's 't' test and χ^2 test were

RESULTS

Table I: Age and Sex Distribution in Controls and Cases

Groups	Sex	Number (%)	Mean (SD) Age in Years
Controls	Male	20 (66.6)	52±6.88
	Female	10 (33.3)	
Cases	Male	20 (66.6)	50±6.33
	Female	10 (33.3)	
	t= 0.879, df=1, p> 0.05		

Table II: Risk Factor Distribution among Controls and Cases

Risk Factor	Controls (%) (n=30)	Cases (%) (n=30)	χ^2	df	p value
Hypertension	04 (13.3)	14 (46.7)	7.937	1	<0.01
Diabetes Mellitus	04 (13.3)	18 (60.0)	14.067	1	<0.001
Smoking	05 (16.7)	13 (43.3)	5.079	1	<0.05
Tobacco chewing	02 (6.7)	05 (16.7)	1.456	1	>0.05

Sedentary lifestyle	04 (13.3)	16 (53.3)	10.800	1	<0.001
Family H/o IHD	03 (10)	05 (16.7)	0.577	1	>0.05

Traditional risk factors for cardiovascular disease were studied among cases and controls.14 cases and 4 controls were hypertensives. The difference was highly significant (p<0.01).There was highly significant difference in diabetes mellitus among cases and controls with 18 diabetics among cases and 4 among controls (p<0.001).There were significantly greater numbers of smokers among cases 13, as compared to controls 2 (p<0.05).There was no significant difference among cases and controls with respect to tobacco chewing with 5 among cases and 2 among controls.

5 cases and 4 controls had family history of IHD and this difference was not statistically significant.16 cases had sedentary life style as compared to 4 among cases. This difference was statistically significant (p<0.001)

Table III: Distribution of cases according to Angiographic findings

Angiographic findings	Cases (%)
Single Vessel Disease	11 (36.7)
Double Vessel Disease	11 (36.7)
Triple Vessel Disease	08 (26.6)
Total	**30 (100)**

Table IV: Table showing the mean values of the risk factors studied.

Sl. No.	Particulars	Cases (Mean±SD)	Controls(Mean± SD)	Significance
1.	hsCRP	2.0±1.4	0.8±0.7	<0.001
2.	TC	221.7±54.8	189.2±29.7	<0.01
3.	TG	225.8±92.3	175.5±56.3	<0.05
4.	HDL-C	30.4±8.1	37.09±8.4	<0.001
5.	LDL-C	149.4±57.1	112.3±37	<0.01
6.	VLDL-C	44.5±18.3	38±12	>0.05
7.	BMI	26.6±1.9	23.5±1.6	<0.001
8.	FBS	131.2±55.9	103.9±26.8	<0.05
9.	PPBS	198.2±71.5	141.6±36.5	<0.001

The mean hsCRP among cases was 2.0±1.4 as compared to 0.8±0.7 among controls. There was highly significant difference in hsCRP among cases and controls (p<0.001).

The mean total cholesterol among cases was higher 221.7±54.8 as compared to controls 189.2±29.7. This difference was highly significant (p<0.01). There was significant difference in triglycerides levels among cases, 225.8±92.3 as compared to controls, 175.5±56.3. The mean HDL among cases was lower, 30.4±8.1 as compared to 37.09±8.4 among controls. This difference was highly significant.

There was highly significant difference in mean LDL Cholesterol levels between cases 149.4±57.1 and controls 112.3±32 (p<0.01). There was no significant difference in VLDL levels among cases 44.5±18.3 and controls 38±12 (p>0.05).

The mean FBS among cases was higher 131.2±55.9 as compared to controls 103.9±26.8 and this difference was statistically significant. There was highly significant difference in PPBS among cases 198.2±71.5 and controls 141.6±36.5.There was no significant difference in serum urea values among cases and controls, with mean serum urea of 24.4±7.3 among cases and 22.3±5.5 in controls. There was no statistically significant difference in serum creatinine value among cases and controls with each group having mean value of 1.0±0.2There was no correlation between hsCRP and total cholesterol in both cases and controls. There was no Correlation between hsCRP and Triglycerides in both controls and cases. There was no correlation between hsCRP and HDL cholesterol in controls and some correlation in cases (r=0.466).There was no Correlation between hsCRP and LDL Cholesterol in both controls and cases. There was no correlation between hsCRP and VLDL Cholesterol in both controls and cases.

DISCUSSION:

Prospective epidemiological studies have identified several independent coronary risk factors including smoking, dyslipidaemia, hypertension and diabetes mellitus.[6] However half of all myocardial infarctions occur in persons in whom plasma lipid levels are normal.[7] With the recognition that atherosclerosis is an inflammatory process, several plasma markers of inflammation have also been evaluated as potential tools for prediction of the risk of coronary events.[5]Several acute phase reactants, cytokines, and soluble cellular adhesion molecules have been implicated in this process, with their plasma concentrations increased in a variety of atherosclerotic disease.[4] Furthermore, several prospective studies have shown that CRP is a predictor of increased risk for MI, stroke or peripheral vascular disease in asymptomatic individuals with no known coronary heart dieses.'[8, 5,]

Moreover, in the Physicians Health study, among low-risk individuals, CRP levels within the normal range were linearly related to the incidence of myocardial infarction over a follow-up period of 8 years.[78]In addition a few studies support the hypothesis that markers of inflammation significantly increase the predictive value of lipid screening.'[9,10]In view of these findings a study was conducted to evaluate the predictive value of CRP as a risk factor in cardiovascular disease and the relation between the levels of CRP and lipid parameters In the present study 66.6% of the study subjects were males and 33.3% were females. The mean age in cases was 50±6.33 years and that in controls were 52±6.88. In a study done by Nader Rifai in 1997 in Boston the mean age in cases was 50.9±9.7.[4] In a study done by Auer et al in Austria the mean age of subjects with CAD was 62.5 years.[11] It can be seen that Cardio Vascular Disease in India is occurring a decade earlier than in developed countries.[12]

In a study done by Kunihiro Kinjo et al, men constituted 74.9% of the total study subjects.[11] Male:female ratio in the present study is similar to that in the earlier studies.

In the present study, 46.7% of cases had the history of hypertension as compared to 13.3% among controls. The study by S Bhagat et al[13] (55% in women), Paul M Ridker et al,[10] (55.8%) present a similar trend of incidence. The hypertension is one of the strong risk factor for cardiovascular disease.

In the present study 60% of cases and 13.3% of controls were diabetic. This difference was highly significant (p<0.001). Similar findings were observed in variouStudies, 48% in cases in a study by Bhagat et al,[13] 12% among cases and 0% among controls in a study by Nader Rifia et al[4] and 6.4% in cases and 1.4% in controls in a study by P. M. Ridker et al.[14]Diabetes mellitus(DM) is an established risk factor in CAD. The role of DM in endothelial dysfunction has been proven beyond doubt.

43.3% of cases and 16.7% of controls had an history of smoking. Similar observations were made by John Danseu et al[64] (58% and 49% among cases and controls respectively). The prevalence of tobacco chewing was low among both cases and controls. This could be because the study was set up in an urban setting and the habit of tobacco chewing is more common in rural areas than in urban areas.

There was significant difference in BMI between cases and controls 26.6±1.9 kg/m^2, 23.5±1.6 kg/m^2 respectively. Similar results were seen in studies conducted by Paul M. Ridker et al [39] and John Danesh et al.[15]

In our study the hsCRP values are significantly higher in patients of coronary artery disease (2.0±1.4 mg/dl) as compared to controls (0.8±0.7 mg/dl). Based on various studies it has been demonstrated that individuals without inflammation usually have CRP levels below 1 mg/dl. Patients with CRP levels between 1 and 3 mg/dl have intermediate risk and above 3 mg/dl have high risk of CAD.[14]

However in patients with CRP levels more than 10 mg/dl other causes of inflammation must be sought for. Thus with this in view, estimation of hsCRP plays an important role in cardiovascular risk detection.

In the present study 20 among 30 cases had hsCRP above 1 mg/dl as compared to 9 among 30 controls. Moreover 6 cases had hsCRP value above 3 mg/dl and none among controls. This data suggests a strong correlation between high hsCRP and CAD. Various studies done across the world have projected similar results.

Nader Rifia et al[4] in their study on men with angiographically documented CHD, there was a highly significant (p<0.0001) difference in CRP values between cases and controls. Mean CRP value among cases was 3.4 mg/l as compared to 1.5 mg/l among controls.

John Danesh et al[15] have reported that the odds ratio for CHD was 1.93 among patients with CRP value above 2.0 mg/liter as compared to patients with CRP value below 0.78 mg/lit. They conducted a meta

analysis of 22 different studies involving a total of 7068 patients with mean follow up of 12 years. The overall odds ratio for CAD value in upper three-quartile range as compared to patients in first quartile.[15]

Studies by Frils Haverkate et al has shown that the relative risk of coronary artery event was about two times greater in the fifth quartile of CRP concentration than in first four quartiles.[16]S. Bhagat et al conducted a prospective study on 44 subjects of unstable angina and 40 controls over a period of 12 months. The mean CRP level in study group was significantly higher - 6.12±6.134 mg/l as compared to control group 1.52±0.75 mg/l (p=0.00). 95.5% of the study group had CRP level more than 2 mg/l while 72.5% of controls had CRP level < 2mg/l.

In a study done by the Paul M. Ridker et al 27,939 women above 45 years of age were studied with a follow up period of 8 years. The outcome studies were first cardiovascular event. The relative risk of first cardiovascular event was 2.3 in women in fifth quintile range of CRP as compared to first quintile.[10]The mean CRP in cases was significantly higher 6.45 mg/l as compared to controls 3.75 mg/l (p<0.0001).

Christopher Bickel et al conducted follow up study on angio graphically proven CAD. The outcome measured was death due to CAD. The mean CRP was significantly higher 2.9 mg/l in patients who dies of cardiac causes than among those who did not 1.3 mg/l.In the present study, the mean total cholesterol, triglycerides and LDL cholesterol levels were significantly greater in cases as compared to controls. The mean HDL-cholesterol was significantly lower in cases. However there was no significant difference in mean VLDL levels between cases and controls (p>0.05).Dyslipidaemia has been proven as one of the major risk factor for CHD. Both VLDL – cholesterol and LDL-cholesterol are associated with atherogenic process, and there is increasing evidence that HDL-cholesterol prevents atherogenesis. The current trend in management of dyslipidaemia is based on the executive summary of the third report of the National Cholesterol Education Program (NCEP). Accordingly the basic principle of prevention of the intensity of risk reduction should be adjusted to person's absolute risk. This involves identification of all the risk factors associated with CHD in a patient. The cutoff values for lipid parameters depends on the total risk factors present.[17]In line with the present study case control studies reported within India have also reported high total cholesterol, HDL cholesterol and triglyceride levels in patients suffering from CHD. Vashist et al from Delhi studied 702 clinically documented CHD and 186 normal healthy controls and reported that total LDL-cholesterol, and triglyceride levels were significantly higher in cases while HDL cholesterol level was not different.[18]Paul Ridker et al in their study did a comparison of LDL-cholesterol and CRP among apparently healthy women. They found minimal correlation (r=0.08) between LDL cholesterol and CRP.[10]In another study on healthy men by Paul Ridker, it was observed that evaluation of CRP added to the predictive value of lipids on risk of first MI. It was seen that patients with highest tertile of both TC and CRP had relative risk of first MI 5.3 times more than that of individuals in lowest tertile of both parameters.[19]There was no significant difference in blood urea and serum creatinine levels in both cases and controls, and it was within normal limits. Similarly urine albumin was absent in all the subjects among the cases as well as controls.From the above results we can infer that hsCRP is significantly higher in CAD cases. Thus, can be used as a risk factor for CAD. TC, TG, HDL and LDL-C levels are significantly elevated in cases. On testing for correlation between hsCRP and various lipid parameters, there was some association between hsCRP and HDL-cholesterol.

CONCLUSION

The study thus suggests that hsCRP level appears to be a dependable marker of Coronary artery disease.Thus, hsCRP can be used as a sensitive predictor of CAD.

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Permission from IRB: Yes

Abbreviations: hsCRP: High sensitivity C-reactive protein, CAD: Coronary Artery Disease

REFERENCES

1. Harvey S. Hecht, Atherosclerotic risk factors revisited. The American Journal of Cardiology. 2004 Jan; 93:73-75.
2. Marcello Rattazi, Massimo Puato, Elisabetta Faggin.et.al. C-reactive protein and interleukin-6 in vascular disease; culprits or passive bystanders? Journal of Hypertension, 2003; 21(10): 1787-1803.
3. Dominick J Angiolillo, Luigi M Biasuci, Giovanna Liuzzo.et.al. Inflammation in acute coronary syndromes; mechanism and clinical implications. Rev. Esp Cardiol, 2004; 57 (5): 433-46.
4. Nader Rifai, Rana Joubran, Harry Yu.et.al Inflammatory markers in men with angiographically documented coronary heart disease. Clinical Chemistry 1999; 45(11): 1967-1973.
5. Paul M Ridker, Charles M Hennekens, Julie E Buring.et.al C-reactive protein and other markers of inflammation in the prediction of cardiovascular disease in women. N. Eng J. Med, 2000 March; 342(12): 836-43.
6. Wilhelmen L, Wedel H, Tibblin G. Multivariate Analysis of risk factors for coronary heart disease. Circulation. 1973; 48; 950-958.
7. Braunwald E. shattuk. Lecture – cardiovascular medicine at the turn of millennium: Triumphs, concerns, and opportunities. N Eng J Med 1977, 337: 1360-1369.
8. Ridker P M, Cushman M, Stampfer M J.et.al. Inflammation, aspirin, and the risk of cardiovascular disease in apparently healthy men. N Eng J Med 1997; 336: 973-979.
9. Ridker PM, Rifai N, Rose L et al, Comparison of C-reactive protein and low density lipoprotein cholesterol levels in prediction of first cardiovascular events. N Eng J Med, 2002; 347: 1557-1565.
10. Paul M Ridker, Julie E Buring, Jessie Shih et.al.Prospective study of c-reactive protein and risk of future cardiovascular events among apparently healthy women. Circulation 1998; 98: 731-733.
11. Auer J, Rammer H, Berent R, Weber T.et.al Relation of c-reactive protein levels to presence, extent and severity of Angiographic coronary artery disease. Indian Heart Journal 2002; 54: 284-88.
12. K Park. Parks Text book of Preventive and Social Medicine. 16th edition.M/s. Banarasidas Bhanot Publishers. Jabalpur (India): 270-280.
13. S. Bhagat, M Gaiha, CK Sharma.et.al. A comparative evaluation of C-reactive protein as a short-term prognostic marker in seven unstable angina – A preliminary study JAPI 2003 April; 51: 349-54.
14. Edward T.H. Yeh, James T Willerson; Coming of Age of C-reactive protein using inflammation markers in cardiology. Circulation 2003; 107: 370-372.
15. John Danesh, Jeremy G Wheeler, Gideon M Hirschfield.et al; C-reactive protein and other circulating markers of inflamation in the prediction of coronary heart disease. N Engl J Med, 2004 Apr; 350 (14); 1387-97.
16. Frits Haverkate, Simon G Thompson, Stephen DM Pyke.et.al. Production of C-reactive protein and risk of coronary event in stable and unstable angina. Lancet 1997; 349: 462-66.
17. Expert panel on detection evaluation and treatment of high blood cholesterol in adults. JAMA, 2001 May; 285 (19): 2486-2497.
18. Vashist S, Narula J, Awtade A.et.al. Lipids and lipoproteins in normal controls and clinically documented coronary heart disease patients. Am Natl Acad Med Sci 1990; 26: 57-66.
19. Paul M Ridker, Robert J Glynn, Charles M Hennckens, C-reactive protein adds to the predictive value of total and HDL cholesterol in determining risk of first myocardial infarction. Circulation, 1998; 97: 2007-2011.