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C-REACTIVE PROTEIN AND HOMOCYSTEINE RISK PREDICTION IN CORONARY ARTERY DISEASE

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ABSTRACT

Background   Elevated levels of C-reactive protein (CRP) and Homocysteine are associated with increased risk for incident Coronary artery disease on the basis of observation from several prospective epidemiological studies*.* *Method* We measured CRP and Homocysteine in 100 subjects which included 50 patients with confirmed CAD and 50 healthy age   matched subjects as control. Homocysteine and CRP were associated with most traditional cardiovascular risk factors. *Result*   Mean value of serum homocysteine level of CAD patients is 35.24±17.804 µmol/l, which was significantly elevated [p< 0.001]than control group with mean value of 9.192± 3.0618 µmol/l and serum C-RP level was also significantly elevated [p< 0.001] in patients of CAD 3.72± 2.5856 mg/dl compare to control [0.808± 0.3746mg/dl]. *Conclusion*   In a large population based samples, subjects with higher CRP and Homocysteine levels had a modest increase in the prevalence of CAD.

INTRODUCTION

The situation of coronary heart disease in India is quite alarming. Reddy reported that mortality from cardiovascular diseases was projected to decline in developed countries from 1970 to 2015 while it was projected to almost double in the developing countries [1]. In the Global Burden of Disease Study it was reported a total of 9.4 million deaths in India in 1990, cardiovascular diseases caused 2.3 million deaths (25%), 1.2 million deaths were due to CHD and 0.5 million deaths due to stroke. It has been predicted that by 2020 there would be 111% increase in cardiovascular deaths in India. This increase is much more than 77% for China, 106% for other Asian Countries and 15% for economically developed countries. The incidence of coronary heart disease in any population is associated with the relative shifts in its biological characteristics-serum lipids, blood pressure, blood glucose, insulin, thrombogenic factors and others. This hypothesis is based on Pickering's observation that sick individuals are just the extreme of a continuous distribution and Key's postulation of sick individuals and sick populations [2].   These shifts are a consequence of changes in lifestyles-smoking, physical activity, alcohol intake and rich diet as well as psychosocial influences that accompany economic transition. It has recently been discovered that elevated plasma levels of the

Amino acid homocysteine are associated with a greater risk and increased mortality form CAD in the general population. However, before homocysteine can be definitely established as a risk factor for the disease many questions remain to be answered such as whether elevated homocysteine levels to lead to CAD, or vice versa. Elevated plasma homocysteine may be an important cause for atherosclerosis formation [3]. The adverse effects of homocysteine, involve oxidative damage to vascular endothelial cells, increased proliferation of smooth muscle cells, and oxidative modification of low density lipoprotein, all leading to atherosclerosis [4]. C-reactive protein is a liver-derived pattern recognition molecule that is increased in inflammatory states. It rapidly increases within hours after tissue injury, and it is suggested that it is part of the innate immune system and contributes to host defense. Since cardiovascular disease is at least in part an inflammatory process, CRP has been investigated in the context of arteriosclerosis and subsequent vascular disorder.CRP a marker of inflammation that has been shown in multiple prospective epidemiological studies to predict incident myocardial infarction, stroke, peripheral arterial disease and sudden cardiac death. CRP composed of five 23kDa subunits, C-reactive protein is a hepatically derived pentraxin that plays a key role in the innate immune response, CRP has a long plasma half-life and is now understood to be a mediator as well as a marker of atherothrombotic disease. To date, over a dozen prospective epidemiological studies carried out among individuals with no prior history of cardiovascular disease

demonstrate that a single, non-fasting measure of CRP is a strong predictor of future vascular events [5].

There is intense interest in the relationship between inflammation and cardiovascular diseases, especially acute cardiovascular events. of all the inflammatory markers for cardiovascular disease. CRP is considered to be one of the most important markers and has been extensively studied in recent years. A meta-analysis of prospective studies of general populations reported that a higher CRP level was related to a 58% increase in the incidence of cardiovascular diseases, which indicated that CRP was a moderately valuable marker in predicting the development of cardiovascular disease [6].

MATERIALS AND METHODS

This descriptive study was conducted in Department of Biochemistry and Medicine in Prince Bijaysingh Memorial [PBM] Hospital associated with Sardar Patel Medical College, Bikaner . The present study was conducted on 100 subjects aged between 35to60years, comprising of 50 normal control and 50 patients suffering from CAD as study group. The patients with renal disease, liver disease, diabetes mellitus, respiratory failure and those on drugs influencing the homocysteine level were excluded from this study. A fasting blood sample was taken from all the patients and controls for the estimation of homocysteine and C-RP. Homocysteine was assayed by using high pressure liquid chromatography apparatus equipped with electrochemical detector as describe by J L D'Eramo et al [7]. Here sodium borohydride (NaBH$_4$) was used as a reductant and 0.1M monochloroacetic acid and 3.6mM sodium octylsufate adjusted to pH 3.2 was used as the mobile phase. All the reagents used were of HPLC grade. . C-RP was estimated in serum by latex agglutination method using C-RP latex kit.

Statistical analysis: All the values calculated as mean ± standard deviation. The two groups were analyzed by comparing each parameter by students- t test. The diagnostic statistics namely, sensitivity, specificity, positive predictive value, negative predictive value, accuracy, odds ratio and kappa were calculated for finding the diagnostic values of CHD risk factors. P values were computed using 'chi square' distribution.

RESULTS

Table 1 shows the mean and SD value of serum homocysteine level of CAD patients and control subjects.. Homocysteine was increased significantly (p<0.0001) in serum of CAD patients when compared to controls. Table 2 shows C-RP levels in CAD patients and control group .C-RP was increased significantly (p<0.001) in serum of CAD patients when compared to control group. The results were also represented by graphs. Graph 1 and 2 represent respectively datas of homocysteine and c-rp in control as well as study group.

Table 1 : Indicates Homocyteine level in CAD patients and control group

Homocysteine	No. of cases	Mean	S.D.
Control	50	9.192	3.0618
CAD Patients	50	35.24	17.80461
p value	<0.001		
t value	10.19		
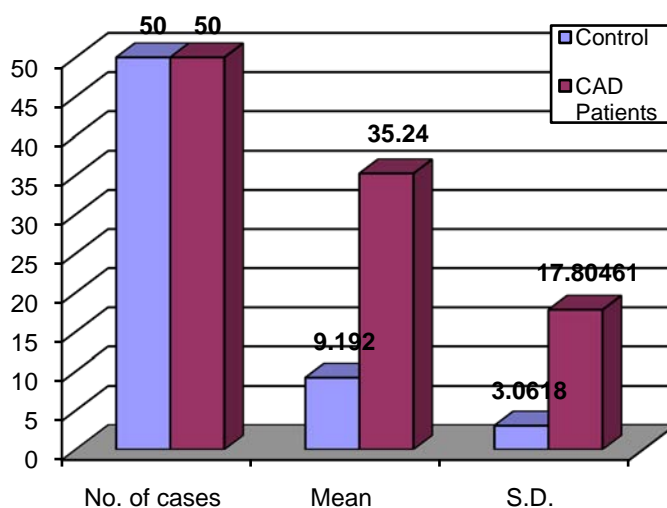
Table: 2 Indicates CRP level in CAD patients and control group

C.R.P.	No. of cases	Mean	S.D.
Control	50	0.808	0.3746
CAD Patients	50	3.72	2.5856
p value	<0.001		
t value	7.89		
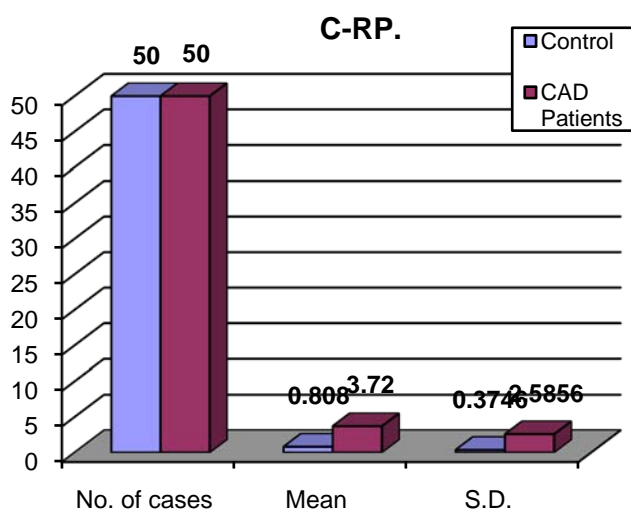
Graph 2: Shows CRP level in CAD and control group

DISCUSSION

The present study shows significantly increased serum homocysteine level in CAD patients as compared to control subjects. The mean serum homocysteine level was found to be increased to 35.24±17.80µmol/l with a range of 10-14 µmol/l in patients of CAD (table no.1). The results were in close conformity with the findings of Yadav et al [8] and Tahir et al [9]. The mean serum homocysteine level was observed to be 9.19±3.06µmol/l with a range of 5 - 15µmol/l in normal control subjects (table no.1).The results were in close collaboration with the observation made by Jaffrey et al [10]. Since 1992 there are several studies indicating that elevated homocysteine was an independent graded risk factor for athersclerotic disease in coronary, cerebral and peripheral arteries [11]. C-reactive protein (CRP) is a liver-derived pattern recognition molecule that is increased in inflammatory states. It rapidly increases within hours after tissue injury, and it is suggested that it is part of the innate immune system and contributes to host defense. Since cardiovascular disease is

at least in part an inflammatory process, CRP has been investigated in the context of arteriosclerosis and subsequent vascular disorders. Lagrand et al [12] determined that serum C-RP level is very highly significant (p<0.001) when compared to control subjects. Aaron et al [13] determined the elevated serum C-RP concentration in atherosclerotic patients. Beamer et al [14] have also reported that stroke patients without infection have increased level of C-RP.

The present study shows that mean C-RP level was found to be 0.80±0.37mg/dl with a range of in control subjects (table no.2). These results are in close agreement with the finding of Ridker et al [15]. The mean serum C-RP level was increased to 3.72±2.58mg/dl with a range of 1.12 to 2.24mg/dl in a patient of CAD as shown (table no. 2). The increase was statistically significant as evident by P value (P=0.0001) as shown (table no.2). The result of present series of study resembled with finding of Jaswal et al [16]. The rise in C-RP concentration in patients of study group was found to be significantly elevated as evident by P value (table no.2). The results of present studies are in collaboration with result of 6.14±4.02mg/dl which measured by Jaffery et al [10]. Fruchart et al [17] also showed that serum homocysteine may be an important cause for atherosclerosis formation. Chambers est al [18] reported that serum homocysteine is an independent risk factor for CAD in asians as compared to europeans. Hennekens et al [19] also showed that serum homocysteine and C-RP level increased in CAD patients.

CONCLUSION

The present studies show that Serum Homocysteine level is significantly elevated in CAD patients as compared to controls. Serum C-RP level in CAD patients is also significantly elevated as compared to controls. Our findings suggest that early CRP and Homocysteine is a valuable prognostic marker for patients with CAD.

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