Original Research Article

Compare and correlate the levels of lipoprotein (a) and high-sensitive C-reactive protein in coronary heart disease with control

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ABSTRACT

Background: The incidence of ischemic heart disease/ myocardial infarction is rapidly increasing in India. However, the traditional risk factors alone could not explain this excess of Coronary Heart Disease (CHD). So, we are in need of a tool to assess the severity and prognosis of these acute coronary syndromes. Lipoprotein (a) [Lp(a)] and High Sensitive C-Reactive Protein (hs-CRP) have been recognised as independent risk factors for CHD in many retrospective case control studies. As the data shows inconsistency in the prediction of risk by Lp(a) and hs-CRP, the study is carried out to compare and correlate the levels of Lp(a) and hs-CRP in coronary heart disease patients with controls.

Methods: An observational case control study was conducted at Maharaja's Institute of Medical Sciences, Nellimarla, with 120 participants. 80 admitted with CHD were categorised as type 2 diabetic and non-diabetic. Remaining 40 participants were age matched controls, who have attended the OP for general health check-up. Samples collected from the participants were analysed for Lp(a), hs-CRP and HbA1c.

Results: Lp(a) levels were significantly elevated in CHD patients with diabetes (69.2±27.5) and non-significant in CHD patients without diabetes (50.4±24.3) as compared to their controls (36.6±22.5). There was significant correlation and elevation of hs-CRP in CHD patients with diabetes (6.0±2.6) and without diabetes (3.7±2.0) as compared to their controls (0.7±0.4).

Conclusions: The present study shows a lack of association of Lp(a) levels in CHD patients with and without diabetes. A strong correlation of the inflammatory marker, hs-CRP was observed between the CHD patients with and without diabetes and even as compared to their controls. It may be concluded that hs-CRP is a better and independent marker than Lp(a) in patients with CHD.

Keywords: Coronary heart disease, High-sensitive C-reactive protein, Lipoprotein (a), Myocardial Infarction

INTRODUCTION

Acute Myocardial Infarction (AMI) is the overwhelmingly the most important form of Ischemic Heart Disease (IHD), which continues to be the leading cause of death and disability in the world and incurs a greater economic burden than any other illnesses.[1] In the industrialized and developing countries like India, despite spectacular progress in their prevention, detection and treatment over the last 3 decades, a steady escalation in the prevalence of Coronary Heart Disease (CHD) is observed.[2] With rapidly increasing urbanization and sedentary life style the incidence of IHD is on an increase in India.[3]

A large number of asymptomatic individuals by the time they develop the clinical manifestations of CHD including the cardiac death, the atherogenic process is far

advanced.[4] About one third of patients with AMI die before reaching the hospital to receive any effective treatment.

The predilection to CHD is attributable to various risk factors which include the life style modifiable factors such as smoking, obesity, physical inactivity and those by life style and pharmacotherapy include lipid disorders, hypertension and insulin resistance.[5] The unmodifiable risk factors include age, sex and genetics. However, in clinical practice we do find a significant number of patients who develop CHD even in the absence of these established risk factors.[6]

Lipoprotein (a) [Lp(a)] and High-Sensitive C-Reactive Protein (hs-CRP) are increasingly being recognized as an independent risk factors for CHD. Earlier studies have shown Lp(a) being a non-significant risk factor for CHD.[7] But a prospective study conducted in western population has shown a significant elevation of Lp(a) in patients with CHD as compared to their controls.[8] Amongst the markers for vascular inflammation, hs-CRP has been found to be most credible, consistent and sensitive in numerous studies conducted at various centres all over the world.[9] During inflammatory reaction, inflammatory cytokines are released from inflamed tissue, which stimulate liver to synthesise a number of acute phase proteins including hs-CRP. But still Lp(a) and hs-CRP are not being used widely for assessing the risk of CHD.[10] Scarcity of statistics, scattered population and difference in ethnicity might be the reasons for inconsistency in the prediction of risk for CHD by Lp(a) and hs-CRP.[11] So the present study is carried out to compare and correlate the levels of Lp(a) and hs-CRP in CHD patients with controls.

METHODS

The study was an observational case control study. Study was conducted at Maharaja's Institute of Medical Sciences, Nellimarla, from February 2018 to January 2019, among the people attending the Out-Patient (OP) and In-Patient (IP) departments. Informed consent in local language was taken from all the participants. IEC clearance was obtained.

Sample size

Total 120 participants were selected. Out of 80 patients admitted with Coronary Heart Disease (CHD) 40 were type 2 diabetic and others were non-diabetic. Remaining 40 participants were age matched controls, who have attended the OP for general health checkup during the study period.

Inclusion criteria

Patients admitted with CHD with or without diabetes based on the American Diabetes Association (ADA) guidelines.

Exclusion criteria

Patients with chronic liver diseases, hypothyroidism, end stage renal disease, systemic infection and those taking drugs which affect the levels of Lp(a) and hs-CRP.

Method of data collection

The following data is collected from all the participants. Baseline data includes name, age, sex, occupation, weight, height, personal history, family history and drug history. Other investigations include Lp(a), hs-CRP, HbA1c, Total cholesterol, Triacylglycerols, HDL-Cholesterol and LDL- Cholesterol.

Statistical analysis

p values <0.05 are considered significant. All the values are calculated as mean±SD. Student 't' test and Fisher F test are used to find the statistical significance. SPSS software is used for data analysis.

RESULTS

The study was conducted at Maharaja's Institute of Medical Sciences, Nellimarla with 120 participants. 80 participants were admitted with CHD, in which 40 patients were of type 2 diabetic as per the American Diabetic Association (ADA) guidelines and remaining 40 were non diabetic.

Table 1: Comparison between controls and CHD patients with type 2 diabetes.
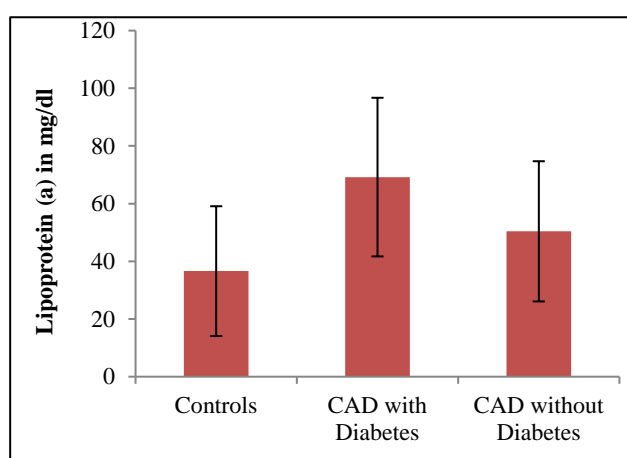
Parameter	Controls	CHD with diabetes	P value
Age (years)	44.2±4.3	48.5±6.0	0.087
Lipoprotein (a) (mg/dl)	36.60±22.5	69.2±27.5	0.009*
High sensitive C-reactive protein (mg/L)	0.7±0.4	6.0±2.6	<0.001*
HbA1c (%)	5.0±0.8	7.9±2.3	0.001*
Total cholesterol (mg/dl)	161.8±5.7	231.0±50.4	0.002*
Triacylglycerols (mg/dl)	129.3±34.0	179±36.6	0.005*
HDL-cholesterol (mg/dl)	44.7±7.9	38.2±9.1	0.106
LDL-cholesterol (mg/dl)	104±29.9	155.1±29.3	0.001*

Data are mean±SD unless otherwise mentioned; P <0.05 is significant.

The other 40 were age matched controls, who had attended the OP for general health checkup during the study period. Samples were collected from all the participants and assessed for Lipoprotein (a), High-

Sensitive C-reactive protein, HbA1c, total cholesterol, HDL-cholesterol and LDL-cholesterol levels.

Table 1 shows comparison of controls with CHD in type 2 diabetic patients. Lp(a) levels were significantly (p=0.009) elevated in CHD patients with type 2 diabetes (69.2±27.5) as compared to controls (36.6±22.5) (Figure 1). hs-CRP, an inflammatory marker is also elevated significantly (p <0.0001) in CHD patients with type 2 diabetics (6.0±2.6), when compared to the age matched controls (0.7±0.4) (Figure 2). HbA1c levels, an indicator of average blood glucose levels in the past three months have risen significantly (p=0.001) in CHD patients with type 2 diabetes as compared to their controls (5.0±0.8). Lipid profile is significantly altered in type 2 diabetics with CHD as compared to the controls (Table 1).

Table 2 gives the relationship between the CHD patients without diabetes and age matched controls. There was a non-significant (p=0.20) elevation in Lp(a) levels in CHD without type 2 diabetes (50.4±24.3) as compared to the controls (36.6±22.5) show the less significance of Lp(a) as marker for CHD patients without type 2 diabetes (Figure 1). Hs-CRP is markedly elevated (p=0.0002) even in CHD without diabetes (3.7±2.0) as compared to their controls (0.7±0.4) (Figure 2). A little significance (p=0.035) was observed in total cholesterol levels and non-significant elevation was observed with HbA1c (p=0.33), Triacylglycerols (p=0.089), HDL-Cholesterol (p=0.117) and LDL-Cholesterol (p=0.249) in CHD patients without diabetes as compared to controls (Table 2).

Figure 1: Lipoprotein (a) levels in CHD patients with and without diabetes compared to their controls.
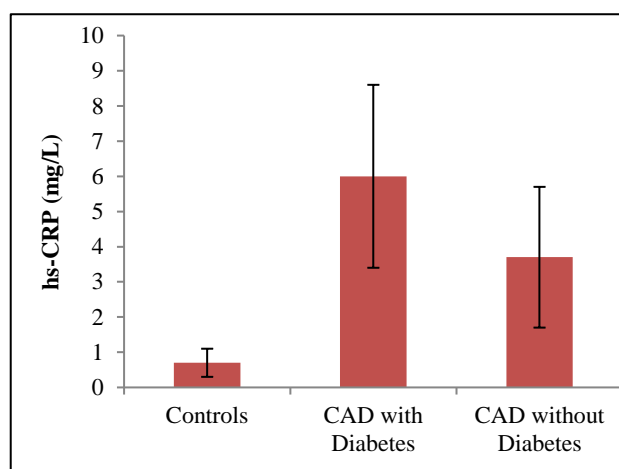
Figure 2: High sensitive C-reactive protein levels in CHD patients with and without diabetes compared to their controls.

Table 2: Comparison between controls and CHD patients without type 2 diabetes.

Parameter	Controls	CHD without diabetes	P value
Age (years)	44.2±4.3	43.2±8.4	0.744
Lipoprotein (a) (mg/dl)	36.60±22.5	50.4±24.3	0.201
High sensitive C-reactive protein (mg/L)	0.7±0.4	3.7±2.0	0.0002*
HbA1c (%)	5.0±0.8	5.4±0.9	0.330
Total Cholesterol (mg/dl)	161.8±35.7	203.7±46.2	0.035*
Triacylglycerols (mg/dl)	129.3±34.0	156.2±33.0	0.089
HDL-cholesterol (mg/dl)	44.7±7.9	39.8±6.44	0.147
LDL-cholesterol (mg/dl)	104±29.9	119.1±25.0	0.249

Data are mean±SD unless otherwise mentioned; P <0.05 is significant.

Table 3: Comparison of CHD patients with and without type 2 diabetes.

Parameter	CHD with Diabetes	CHD without diabetes	P value
Age (years)	48.5±6.0	43.2±8.4	0.123
Lipoprotein (a) (mg/dl)	69.2±27.5	50.4±24.3	0.041*
High sensitive C-reactive protein (mg/L)	6.0±2.6	3.7±2.0	0.006*
HbA1c (%)	7.9±2.3	5.4±0.9	0.021*
Total cholesterol (mg/dl)	231.0±50.4	203.7±46.2	0.147
Triacylglycerols (mg/dl)	179±36.6	156.2±33.0	0.656
HDL-cholesterol (mg/dl)	38.2±9.1	39.8±6.44	0.008*
LDL-cholesterol (mg/dl)	155.1±29.3	119.1±25.0	0.126

Data are mean±SD unless otherwise mentioned; P <0.05 is significant.

CHD patients with and without diabetes was compared in Table 3. A significant variation was observed in hs-CRP (p=0.04), Total cholesterol (0.02), LDL-cholesterol (p=0.008) and HbA1c (p=0.006) in between the CHD patients with and without diabetes. There was no significant difference of Lp(a) (p=0123), Triacylglycerol (p=0.147) and HDL-cholesterol (0.656) in between the two groups (Table 3).

DISCUSSION

Prospective and retrospective studies have suggested an independent association between high levels of Lp(a) and presence of CHD. This association has been documented in men and women in Asian Indians and African Americans.[14] Present study shows that Lp(a) is significantly elevated in CHD patients with diabetes and no significance was observed in CHD patients without diabetes when compared to the controls, which is similar to previous studies conducted by Zheng ye et al.[15] Lp(a) did not correlate with future risk for myocardial infarction or stroke. In Jauhinaien M et al, study base line Lp(a) levels were similar in patients who developed coronary events over 5 years follow up and in those who did not. So Lp(a) cannot be considered an independent risk factor for CHD.[16]

Studies have determined that inflammation plays a significant role in the pathogenesis of atherosclerosis.[17] There are many markers of inflammation as fibrinogen, interleukin-6, complements, hs-CRP but most promising among these is hs-CRP, which is an independent marker of CHD.[18] In the present study hs-CRP is significantly raised in both CHD patients with diabetes and without diabetes when correlated to controls. hs-CRP levels are still higher in diabetes than in non-diabetics which could be because of raised oxidation of lipids, increased glycation end products in diabetic patients. Activated leukocytes in infection/trauma release interleukin-6 which stimulates the formation of hs-CRP, an acute phase reactant. hs-CRP so produced activates the complement pathway, facilitate adhesion of monocytes and recruitment into arterial wall- a critical step in atherosclerosis.[19]

Several studies have demonstrated an association between diabetes and inflammation. The results of our study are in strong agreement with these studies. hs-CRP levels were associated with a two-fold increase in cardiovascular mortality after adjusting for age and sex in Jager A et al, study.[20]

Association between HbA1c (glycemic control) and hs-CRP (systemic inflammation) in present study shows that poor glycemic control is associated with increased inflammation is in accordance with King D et al, study.[21] Total cholesterol, in line with hs-CRP is significantly elevated in both the group, is an important risk factor for CHD with and without diabetes.

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