Research Paper

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The High Sensitivity C-Reactive Protein and Low Density Lipoprotein Cholesterol in Risk Prediction of Ischemic Heart Disease

Biochemistry

KEYWORDS : Atherosclerosis, hs-CRP, Ischemic heart disease (IHD), LDL-C

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ABSTRACT

Background: As atherosclerosis is an inflammatory process and C- reactive protein is considered as a marker of inflammation, this study was designed to evaluate the hs-CRP and LDL-C to find out a better risk predictor of ischemic heart disease (IHD).

Methods: In the present cross sectional study, 100 patients of IHD and 50 apparently healthy subjects were included and fasting blood parameters like lipid profile and hs-CRP were performed. Data were evaluated by applying student t test and sensitivity/specificity were also calculated.

Results: Levels of hs-CRP (p<0.01) and LDL-C (p<0.05) were significantly elevated in IHD patients than the control group but 55 patients of IHD had normal LDL-C, while their hs-CRP levels were significantly high. Furthermore, specificity and sensitivity of hs-CRP were also higher (100% & 97%) as compare to LDL-C (66% & 044%) in patients group.

INTRODUCTION

Compelling evidence exists to support CRP's designation as a powerful independent predictor of future cardiovascular risk. CRP predicts cardiovascular risk in a wide variety of clinical settings, including men and women without overt cardiovascular disease, patients with stable angina or presenting with acute coronary syndromes, postmyocardial infarction patients and those with the metabolic syndrome. (3,4,7,9,12)

Furthermore, CRP predicts not only incident myocardial infarction and cardiovascular death, but also risk of ischemic stroke, sudden cardiac death, incident peripheral artery disease and restenosis after percutaneous coronary intervention. (5,6,11,15) In primary prevention, CRP confers additional prognostic value at all levels of Framingham risk and at all levels of the metabolic syndrome and blood pressure.(1,2,10) In head-to-head comparisons with LDL cholesterol, CRP was found to be the stronger predictor of incident cardiovascular events.(2) This robust association with future cardiovascular events has provided an analytic opportunity for CRP in clinical use. CRP is an appropriate marker because it has a long half-life, its levels remain stable over time without exhibiting circadian variability and fasting blood samples are not required. Currently, CRP levels <1 mg/L, 1 to 3 mg/L, and >3 mg/L are used to denote low-, intermediate-, and high cardiovascular risk groups. (8)

MATERIALS AND METHODS

The present study was conducted at Department of Biochemistry, Govt. medical college & Sir Takhtsinhji General Hospital, Bhavnagar, Gujarat, in which 100 patients of Ischemic Heart Disease (study group) primarily diagnosed by clinical examination and biochemical investigations admitted to the intensive cardiac care Unit (ICCU) and 50 apparently healthy subjects (control group) were included. The study was approved by the Institutional Review Board (Human Ethics committee), Govt. medical college, Bhavnagar and informed consent was obtained from all participants. Fasting blood samples were collected and laboratory investigations like hs-CRP (immunoturbidimetric method), LDL-C (direct method), HDL-C (direct method), total cholesterol (CHOD-PAP enzymatic method), triglyceride (GPO-PAP enzymatic method), plasma glucose (GOD-POD enzymatic method) and Ck-MB (Immunoinhibition UV Kinetic method) were carried out on fully auto analyzer- Miura, A-1005 (ISE-Italy) at NABL (ISO 15189:2007) accredited, Clinical Biochemistry Section, Laboratory services Sir T. Hospital, Bhavnagar.

Graph pad instat 3 demo version software was used for statistical analysis. Descriptive statistics are shown as mean ± standard deviation. Mean levels of all parameyters of case and control groups were compared by unpaired t-test. Normal distribution was tested and data was found to follow normal distribution. *p* value less than 0.05 was considered significant.

RESULTS

Table (1) shows the comparison of hs-CRP and LDL-C in the study group and control group. The mean ages of the groups were not significantly different. It was observed that out of levels of hs-CRP were significantly higher ($p < 0.0001$) in study group as compare to control group, while the levels of LDL-C were also significantly higher in study group in comparison to control group ($p< 0.05$)

Table (2) and (3) shows the comparison between the sensitivity and specificity of hs-CRP and LDL-C. It was found that hs-CRP had 97% sensitivity and 100% specificity whereas LDL-C had only 44% sensitivity and 66% specificity. The results showed that the hs-CRP was more sensitive & specific as compare to LDL-C.

Table 1: Comparison of Control Group & Study Group

Parameters	Biological Reference Interval	Control group (n=50)			Study group (n=100)			Significance (two tailed p value)
		Mini.	Maxi.	Mean ± SD	Mini.	Maxi.	Mean ± SD	
hs-CRP mg/L	0.3- 8 mg/L	0.6	8.0	4.99 ± 2.09	3	290	47.3 ± 64.9	t=4.59 **p < 0.0001
LDL-C mg/dl	80-130 mg/dl	29	218	109 ± 44.03	43	436	132.3 ± 55.9	t=2.57 *p=0.0110

Note: * p < 0.05 = Significant, **p < 0.01 = Highly significant, p >0.0 = Not significant

Table 2: hs-CRP levels in case & control group

hs-CRP	Study	Control	Total
>8	97	0	97
<8	3	50	53
Total	100	50	150

The specificity of the hs-CRP is 1.0 (100%) and the sensitivity is 0.97 (97%).

Table 3: LDL-C level in study& control group

LDL-C mg/dl	Study	Control	Total
>130	44	17	61
<130	56	33	89
Total	100	50	150

The specificity of LDL-C is 0.66 (66%) and sensitivity is 0.44 (44%).

DISCUSSION

In the findings of the present study, Mean age in the study group was 57.8 ±12.58 years and that in control group was 46.3±12.17 years. Total 91% patients were above 40 years of age, the rest of 9% belonged to younger age group. The age incidence of Ischemic Heart Disease indicates that the risk of IHD increases in older age as compare to young age. In a study conducted by Nader Rifai in 1997 in Boston the mean age in cases was 50.9±9. (16)

In a study conducted by Ridker, P.M. (1998), distribution of hs-CRP among apparently healthy American men and women was as given below. (14)

Quintile	range mg/dl	cardio vascular risk estimate
1	0.01 – 0.07	low
2	0.07 – 0.11	mild
3	0.12 -0.19	moderate
4	0.20-0.38	high
5	0.38-1.50	highest

In the present study the levels of hs-CRP in control group were in between 0.3 to 8 mg/L. The mean value in control group was 4.99 mg/L. In study group 97% patients had the level of hs-CRP more than 8 mg/L which indicate marked increase in hs-CRP level in patients of IHD. In a study conducted by Nader Rifia et al. men with angiographically documented CHD, it was demonstrated that there was a highly significant ($p<0.0001$) difference in hs-CRP values between cases and controls. (16) In a case control study conducted by Paul M. Ridker et al. the mean CRP in CHD cases was significantly higher 6.45 mg/L as compared to controls 3.75 mg/L ($p<0.0001$). (13)

The present study was aimed to compare the levels of hs-CRP and LDL Cholesterol in patients of ischemic heart disease (IHD) and to evaluate which one is the better predictor of IHD. The levels of hs-CRP were found to be elevated in patients of IHD and were found highly significant ($p<0.001$) as compare to the control group. The levels of LDL-C in study group were also found to be elevated significantly ($p<0.05$) as compare to the control group.

Accumulating evidence indicates that the hs-CRP is better predictor of IHD than LDL-cholesterol. Recent research on CRP has further established its role as a powerful risk marker for various cardiovascular endpoints in different settings; new potential indications are emerging, and experimental studies have provided new insights in a possibly important direct role of CRP in atherogenesis. This might be of major importance for the advancement of our understanding of atherosclerosis and may open new horizons to combat this far spread disease well in advance and will not only help the cardiologist to limit the CVD complications but improve the quality of life of IHD patients.

CONCLUSION

The study identified that the half of the IHD patients with normal LDL-C levels had significantly elevated levels of hs-CRP. Furthermore, in regard to sensitivity and specificity hs-CRP is far better predictor of IHD than LDL-C. Therefore, hs-CRP should be included in the standard protocol as a better and single predictor of IHD than conventional lipid profile which will improve the physician's ability for the early and better prediction of future occurrence of ischemic heart disease in patients.

REFERENCE

1. Albert, C.M., Ma, J., Rifai, N., Stampfer, M.J. & Ridker, P.M. Prospective study of C-reactive protein, homocysteine and plasma lipid levels as predictors of sudden cardiac death. Circulation. 2002 Jun 4;105(22):2595-9. 7 | 2. Biasucci, L.M., Liuzzo, G., Grillo, R.L., Caligiuri, G., Rebuzzi, A,G, & Buffon, A. et al. Elevated levels of C-reactive protein at discharge in patients with unstable angina predict recurrent instability. Circulation. 1999 Feb 23;99(7):855-60. 3 | 3. Blake, G.J. & Ridker, P.M. C-reactive protein and prognosis after percutaneous coronary intervention. Eur Heart J. 2002 Jun;23(12):923-5. 9 | 4. Blake, G.J., Rifai, N., Buring, J.E. & Ridker, P.M. Blood pressure, C-reactive protein, and risk of future cardiovascular events. Circulation. 2003 Dec 16;108(24):2993-9. 12 | 5. Liuzzo, G., Biasucci, L.M., Gallimore, J.R., Grillo, R,L,, Rebuzzi, A.G. & Pepys, M.B. et al. The prognostic value of C-reactive protein and serum amyloid A protein in severe unstable angina. N Engl J Med. 1994 Aug 18;331(7):417-24. 4 | 6. Ridker, P.M. High-sensitivity C-reactive protein potential adjunct for global risk assessment in the primary prevention of cardiovascular disease. Circulation. 2001 Apr 3;103(13):1813-8. 15 | 7. Ridker, P.M. High-sensitivity C-reactive protein: potential adjunct for global risk assessment in the primary prevention of cardiovascular disease. Circulation. 2001 Apr 3;103(13):1813-8. 11 | 8. Ridker, P.M. Inflammatory biomarkers, statins, and the risk of stroke: cracking a clinical conundrum. Circulation. 2002 Jun 4;105(22):2583-5. 6 | 9. Ridker, P.M., Buring, J.E., Cook, N.R. & Rifai, N. C-reactive protein, the metabolic syndrome, and risk of incident cardiovascular events: an 8-year follow-up of 14 719 initially healthy American women. Circulation. 2003 Jan 28;107(3):391-7. 5 | 10. Ridker, P.M., Hennekens, C.H., Buring, J.E. & Rifai, N. C-reactive protein and other markers of inflammation in the prediction of cardiovascular disease in women. N Engl J Med. 2000 Mar 23;342(12):836-43. 2 | 11. Ridker, P.M., Rifai N, Stampfer, M.J. & Hennekens, C.H., Plasma concentration of interleukin-6 and the risk of future myocardial infarction among apparently healthy men. Circulation. 2000 Apr 18;101(15):1767-72. 1 | 12. Ridker, P.M., Rifai, N., Rose, L., Buring, J.E. & Cook, N.R. Comparison of C-reactive protein and low-density lipoprotein cholesterol levels in the prediction of first cardiovascular events. N Engl J Med. 2002 Nov 14;347(20):1557-65. 10 | 13. Ridker, P.M., Stampfer, M.J. & Rifai, N. Novel risk factors for systemic atherosclerosis: a comparison of C-reactive protein, fibrinogen, homocysteine, lipoprotein(a), and standard cholesterol screening as predictors of peripheral arterial disease. JAMA. 2001 May 16;285(19):2481-5. 8 | 14. Ridker, P.M., Buring, J.E., Shih, J., Matias, M. & Hennekens, C.H. Prospective study of C-reactive protein and the risk of future cardiovascular events among apparently healthy women. Circulation. 1998 Aug 25;98(8):731-3. 16 | 15. Rifai, N., Joubran, R., Yu, H., Asmi, M. & Jouma, M. Inflammatory markers in men with angiographically documented coronary heart disease. Clin Chem. 1999 Nov;45(11):1967-73. 14 | 16. Yeh, E.T. & Willerson, J.T. Coming of age of C-reactive protein: using inflammation markers in cardiology. Circulation. 2003 Jan 28;107(3):370-1. 13 |