International Journal Of

Recent Scientific Research

ISSN: 0976-3031

Volume: 7(11) November -2015

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THE OFFICIAL PUBLICATION OF
INTERNATIONAL JOURNAL OF RECENT SCIENTIFIC RESEARCH (IJRSR)
http://www.recentscientific.com/ recentscientific@gmail.com

ISSN: 0976-3031

Available Online at http://www.recentscientific.com

International Journal of Recent Scientific Research
Vol. 6, Issue, 11, pp. 7185-7187, November, 2015

International Journal of Recent Scientific Research

RESEARCH ARTICLE

ALKALINE PHOSPHATASE AS A POSSIBLE MARKER FOR CORONARY ARTERY DISEASE

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ARTICLE INFO

Article History:

Received 15th August, 2015
Received in revised form
21st September, 2015
Accepted 06th October, 2015
Published online 28st November, 2015

Key words:

ABSTRACT

Introduction: Alkaline phosphatase (ALP) is primarily used as a marker for hepatic or bony diseases. Recent in vitro experimental studies have shown a link between ALP and vascular calcification. ALP catalyzes hydrolysis of organic pyrophosphate which is an inhibitor of vascular calcification. This study was conducted as a step forward to those in vitro experimental findings to look whether ALP has any association with coronary artery disease or not.

Material and Methods: It was a cross sectional study. Triple vessel disease patients (n=31) admitted for bypass surgery were taken as cases and age and gender matched healthy persons were taken as controls (n=30). Serum ALP estimation was done by PNPP kinetic method using the commercially available kit Cobas 10816388 on the automated chemistry analyser Hitachi 912. Data is presented as mean ± SD. Statistical analysis was done on SPSS 21. P-value <0.05 was taken as significant.

Results: The mean ALP level was significantly higher in cases (ALP=228±46.5 IU/L) as compared to controls (ALP=175.6±40.8 IU/L) (p <0.0001). In multiple logistic regression analysis ALP shows a significant and independent association with the prevalence of CAD (p<0.05).

Conclusion: Our result shows an independent association between serum alkaline phosphatase level and coronary artery disease exists. ALP can be considered as a novel marker for coronary artery disease. However, to confirm the findings further prospective studies with larger sample size are needed.

INTRODUCTION

Cardiovascular disorders are the most common cause of morbidity and mortality in India and around the world[1]. Coronary Artery Disease (CAD) constitutes the major fraction of these disorders[2]. CAD is a multifactorial disease with long list of established risk factors. Many patients with CAD do not have any identifiable risk factors, suggesting role of additional factors[3]. Identification of these newer risk factors is an important key for early diagnosis and prevention of CAD. Since vascular calcification is an important phenomenon of coronary atherosclerosis, markers of vascular calcification may harbor potential of predicting CAD. Alkaline phosphatase (ALP) is primarily used as a marker of hepatic or skeletal disorders. Recent studies done in animal models have shown the role of ALP in vascular calcification[4]. Vascular bio-mineralization theory suggests that pyrophosphates(PPi) inhibits the vascular calcification process and ALP increases the vascular calcification by degrading inhibitory PPi[5]. To evaluate these accumulating evidences of role of ALP in CAD, this study was conducted.

MATERIAL AND METHODS

It was a case control study conducted at Vardhman Mahavir medical college and Safdarjung hospital, New Delhi. Thirty one angiographically diagnosed coronary artery disease patients admitted in the Cardio-Thoracic and Vascular Surgery ward for Coronary Artery Bypass Grafting were taken as cases. Sixty healthy individual, matched for age and gender were taken as control. Subjects having acute and chronic renal disorder, liver diseases, skeletal disorders, thyroid disorder, stroke, myocardial infarction in last 6 months, diabetic ketoacidosis, nonketotic hyperosmolar state were excluded from the study. The study was conducted after clearance from ethical committee of Safdarjung Hospital. Proper informed consent was taken from each subjects before including them into the study. Samples were collected after overnight fasting using all standard procedures. Serum ALP estimation was done by PNPP kinetic method using the commercially available system pack kit on the automated chemistry analyzer.The kit was procured from DLD Diagnostika GMBH. The subjects were also screened for Lipid profile, Random Blood Sugar (RBS), Urea, Creatinine, Total Bilirubin, Aspartate Transaminase (AST), Alalnine Transaminase (ALT), Calcium

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and Phosphorus. Statistical analysis was done using SPSS v20.0. Data is presented as mean±SD. The difference in the mean base line values of various parameters was analyzed by unpaired t-test or Mann-Whitney test depending upon whether the values were parametric or non-parametric. Multivariate logistic regression analysis was done to evaluate independent risk factors. ROC curve was plotted to find out critical value of ALP levels as risk factor and Fisher's exact test was done to calculate odd's ratio.

RESULT

Table 1 shows that the mean ALP levels in case group (228.9±46.5 IU/L) is significantly higher than the age and gender matched healthy control group (175.6±40.8 IU/L) (p-value <0.0001).

Table 1 Comparison of baseline characteristics and various parameters between two groups

	Case (n=31)	Control (n=30)	p-value
Age (years)	57.8±7.1	56.5±6.5	0.448
Male:Female	24:7	21:9	0.510
Body Mass Index (kg/m^2)	22.4±2.9	23.3±3.6	0.295
Waist to Hip Ratio	0.84±0.1	0.81±0.12	0.307
Diabetes mellitus	22.5%	-	-
Hypertension	70.9%	-	-
Previous myocardial infarction	12.9%	-	-
Statin user	64.5%	-	-
Smoker	25.8%	-	-
Triglyceride (mg/dl)	163.87±59.38	145.03±100.55	0.0310*
Total Cholesterol (mg/dl)	158.12±53.55	172.63±31.09	0.0541
HDL (mg/dl)	33.58±9.66	43.83±15.61	0.0065**
LDL (mg/dl)	93.09±31.96	117.5±30.12	0.0043**
ALP (IU/L)	228.9±46.5	175.6±40.8	<0.0001***
RBS (mg%)	93.35±9.33	89.86±7.94	0.1180
Urea (mg%)	28.61±9.07	22.12±6.11	0.0034**
Creatinine (mg%)	0.87±0.39	0.65±0.15	0.0056**
Total Bilirubin (mg%)	0.51±0.29	0.4±0.18	0.2149
AST (IU/L)	30.74±14.4	25.26±8.25	0.1743
ALT (IU/L)	29.41±13.35	26.3±15.89	0.1987
Ca (mg%)	8.91±0.78	8.51±0.51	0.0155*
P (mg%)	3.47±0.59	3.55±0.62	0.5249

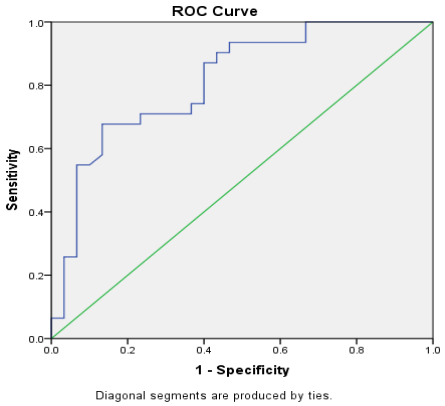

Figure 1 ROC curve to determine cutoff value of ALP

Area Under the Curve				
Test Result Variable(s): ALP				
Area	Std. Error[a]	Asymptotic Sig.[b]	Asymptotic 95% Confidence Interval	
			Lower Bound	Upper Bound
.815	.055	.000	.707	.922

Range of ALP in controls is 114-293 IU/L and in cases it was 148-324 IU/L. Multiple regression analysis in table 2 shows that ALP is independent risk factor of CAD.

Table 2 Multiple regression analysis showing ALP is an independent risk factor

Coefficients[a]					
Model	Unstandardized Coefficients		Standardized Coefficients	t	Sig.
	B	Std. Error	Beta		
(Constant)	140.944	78.073		1.805	0.077
urea	1.520	0.803	0.248	1.892	0.064
creatinine	20.574	15.429	0.172	1.333	0.188
Tg	0.006	0.083	0.010	0.072	0.943
HDL	-0.177	0.507	-0.048	-0.350	0.728
LDL	-0.271	0.198	-0.176	-1.364	0.178
Ca	4.676	8.237	0.074	0.568	0.573
a. Dependent Variable: ALP					

ROC curve analysis in our study shows that cut-off value of 216.5 IU/L can predict the risk of CAD with 67% sensitivity and 87% specificity (Graph1). Fisher's exact test reveals high ALP levels increases the risk of CAD by 2.7 times (95% CI= 1.5 – 4.5) with Odd's Ratio= 13.6; 95% CI=3.7-49.8 (p-value <0.0001). Other baseline characteristics and parameters are summarized in Table1.

DISCUSSION

The effects of serum ALP levels in causing CAD is perhaps mediated by vascular calcification, in which ALP has been shown to be a regulator. Vascular calcification is considered to be an active process mediated by vascular cells and osteogenic factors such as ALP[6]. It has been observed that ALP levels are up-regulated in calcified vessels[7]. ALP regulates vascular calcification through its degrading action on organic pyrophosphate, a potent inhibitor of vascular calcification[6].The evolving theory of ALP causing vascular calcification is well supported by the study of Millan and colleagues showing that blocking the "pyrophosphate degrading action" of alkaline phosphatase reduced the calcification in vascular smooth muscle cells from NPP1- and ANK-deficient mice[4]. It has also been observed that there is independent association between ALP and coronary artery calcification assessed by CT-scan in hemodialysispatients[8]. Since we measured the serum level of tissue-non-specific ALP which is mainly concentrated in the bone, liver, and kidney, in the current study we have excluded the subjects having liver, bone or kidney disease using liver and kidney function test. Bone disorders were excluded using relevant clinical history and measurement of calcium and phosphate levels. Thus, we believe that our findings are unlikely to be limited by significant confounding by liver, bone or kidneydisease. The major drawback of our study is that we didn't measure the isoforms of ALP so it could not be determined which fraction of ALP is increasing the risk of CAD.

CONCLUSION

From the present study it can be concluded that ALP levels are significantly higher in CAD subjects as compared to healthy controls. ALP can be considered as a significant independent risk factor which increases the risk of CAD by 2.7 times.

However, to confirm the findings further prospective studies with larger sample size are needed.

References

1. Celermajer DS, Chow CK, Marijon E, Anstey NM, Woo KS. Cardiovascular Disease in the Developing World: Prevalences, Patterns, and the Potential of Early Disease Detection. J Am Coll Cardiol. 2012;60(14):1207-1216.
2. Fuster V, Kelly BB, editors. Promoting Cardiovascular Health in the Developing World: A Critical Challenge to Achieve Global Health. Washington (DC): National Academies Press (US); 2010. 2, Epidemiology of Cardiovascular Disease. Available from: http://www. ncbi. nlm.nih. gov/books/NBK45688/
3. Nicholls SJ, Wilson Tang WH, Scoffone H, Brennan DM, Hartiala J, Allayee H et al. Lipoprotein(a) levels and long-term cardiovascular risk in the contemporary era of statin therapy J. Lipid Res. 2010; 51(10): 3055- 3061.
4. Narisawa S, Harmey D, Yadav MC, O'Neill WC, Hoylaerts MF, Millan JL. Novelinhibitors of alkaline phosphatase suppress vascular smooth muscle cell calcification.J Bone Miner Res 2007;22:1700–1710.
5. Lomashvili K, Garg P, Narisawa S, Millan J, O'Neill W. Upregulation of alkaline phosphatase and pyrophosphate hydrolysis: Potential mechanism for uremic vascular calcification. Kidney international. 2008;73(9):1024-1030.
6. Shanahan CM, Cary NR, Salisbury JR, Proudfoot D, Weissberg PL, Edmonds ME. Medial localization of mineralization-regulating proteins in association with Monckeberg's sclerosis: evidence for smooth muscle cell-mediated vascular calcification. Circulation 1999; 100: 2168–2176.
7. Park JB, Kang Dy, Yang HM, Cho HJ, Park KW, Lee HY, et al. Serum alkaline phosphatase is a predictor of mortality, myocardial infarction, or stent thrombosis after implantation of coronary drug-eluting stent. European Heart Journal 2013 Mar 21;34(12):920-31.
8. Shantouf R, Kovesdy CP, Kim Y, Ahmadi N, Luna A, Luna C, Rambod M, Nissenson AR, Budoff MJ, Kalantar- Zadeh K. Association of serum alkaline phosphatase with coronary artery calcification in maintenance hemodialysis patients. Clin J Am Soc Nephrol 2009;4 :1106–1114.

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How to cite this article:

Prabhash Bhavsar, Charanjeet Kaur, Jagdish Prasad and Kabi B.C.2015, Alkaline phosphatase as a possible marker for coronary artery disease. *Int J Recent Sci Res. Vol. 6, Issue, 11, pp. 7185-7187, November, 2015*

ISSN 0976-3031