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Research Article

INCREASED SERUM ALKALINE PHOSPHATASE ACTIVITY IN DIFFERENT CARDIAC DISEASES

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ABSTRACT

Introduction: Presently serum ALP activity measurement is used as a marker for bone and liver diseases. In recent research it has been found that the level of ALP activity increases in atherosclerosis and peripheral vascular diseases. Even though at present ALP is not measured for CVD diagnosis but rising evidence showed that increased ALP activity increases CVD risk and its mortality too. At present there are very limited numbers of studies related to ALP activity in CVD. Therefore, we have analyzed serum ALP activity in myocardial infarction, heart failure, rheumatic heart disease, complete heart block, Myocarditis and congenital heart disease patients.

Materials and methods: It was a case control study. 229 cases of CVD (Complete Heart Block-16, Congenital Heart Disease-1, Heart Failure-22, Myocardial Infarction-169, Myocarditis-1, Rheumatic Heart Disease-20) who were admitted in Cardiology ward were taken as cases and age and gender matched healthy persons were taken as controls (n=229). Serum ALP activity estimation was done by PNPP kinetic method using the commercially available kit on fully automated chemistry analyzer. Data is presented as median and inter quartile range (IQR). Statistical analysis was done on SPSS 16.0 and Microsoft Excel. Difference in the level of ALP across the Diagnostic Categories was calculated by Kruskal-Wallis test. P-value <0.05 was taken as significant.

Results: The Median (IQR) ALP level was significantly higher in cases (ALP=210 (95) IU/L) as compared to controls (ALP=187 (23) IU/L) (<0.0005). There was no statistically significant difference in the ALP levels across the diagnostic categories.

Conclusion: Serum ALP activity is significantly increased in different cardiac diseases, which can be considered as a marker in the panel along with other markers for CVD patients. Further research is needed with specific isoenzyme study of ALP in large cohorts and diverse ethnic population, so that can be considered in a panel of marker for cardiovascular risk.

INTRODUCTION

Worldwide, coronary artery disease (CAD) is the main cause of death (1)(2)(3). It is devasting disease where a healthy person may die or become disabled without warning. In this situation if the affected person is below age of 40, leads tragic consequences for family, friends and occupation (4). Burden of CVD is rapidly rising for past 15 years all over world including India (5). In Coronary heart disease, initiation of lipid deposition due to aberrant lipid metabolism takes place in arterial intima with formation of white plaque. Due to which narrowing of vascular lumen occurs and blocking of blood flow takes place. It further leads to cardiac ischemia leading to angina (6). Etiology of CVD is multifactorial where many traditional and nontraditional risk factors are associated (5)(7) suggesting role of additional risk factors (7). For early diagnosis and prevention of CAD newer identified markers can be helpful. In coronary atherosclerosis, vascular calcification is an important incident. For prediction of CAD, markers for vascular calcification will be useful markers. Widely ALP is used as a marker for hepatic and hepatobiliary diseases (7) but its activity increases in atherosclerosis and peripheral vascular diseases (8). Even though currently ALP is not measured for

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CVD diagnosis but rising evidence showed that increased ALP activity increases CVD risk and its mortality too (9).

At present there are very limited numbers of studies related to ALP activity in CVD. With our current knowledge this is the first study in Western Maharashtra population particularly in Mumbai city. Therefore, we have analyzed serum ALP activity in myocardial infarction, heart failure, rheumatic heart disease, complete heart block, Myocarditis and congenital heart disease patients.

MATERIALS AND METHODS

In this study 229 cases of CVD's (Complete Heart Block-16, Congenital Heart Disease-1, Heart Failure-22, Myocardial Infarction-169, Myocarditis-1, Rheumatic Heart Disease-20) who were enrolled at Cardiology and Medicine department from Lokamanya Tilak Municipal General Hospital, Sion, Mumbai were studied. Along with that 229 age and sex matched healthy controls were included in a case control study. Study was approved by Institutional Ethics Committee, Lokamanya Tilak municipal Medical College and General Hospital, Sion. Blood samples were collected from August 2015 to June 2016. All the cases were diagnosed by Cardiologists and final patient selection was done. Diagnostic test done were 2D Echo along with electrocardiogram and final selection of the patients were done with questionnaire to patient. Mean age for cases was 54.49 years and for controls 54.03 years. Patients with chronic illnesses such as liver diseases, bone diseases, pregnant woman, malignancies, infections, rheumatic arthritis were excluded where the level of ALP are presumed to be raised. The serum ALP activity was measured by PNPP kinetic method using the commercially available system pack kit on the automated chemistry analyzer. Statistical analysis was carried out using SPSS version 16.0 and Microsoft Excel.

RESULT

Table 1 Comparison of baseline characteristics and serum level of ALP activity between two groups

	Case (n=229)	Control (n=229)	p-value
Age (years)	54.49±11.71	54.03±12.35	0.636
Male	161 (70.3)	171 (74.7)	-
Female	68 (29.7)	58 (25.3)	-
Body Mass Index (kg/m2)	24.43 (3.61)	25.74 (3.19)	<0.0005
Blood pressure Systolic	122.97 (18.98)	–	–
Diastolic	77.32 (11.32)	–	–
Diabetes mellitus	30.1%	-	-
Hypertension	42.8%	-	-
Previous myocardial infarction	20.5%	-	-
Smoking	24%	-	-
Tobacco	37.1%	-	-
Alcohol	17.5%	-	-
ALP IU/L	Median (IQR) 210 (95)	Median (IQR) 187 (23)	<0.0005*

*Using Mann-Whitney U test, significant at 0.05 level of significance

Table 1 shows that the level of median (IQR) serum ALP activity was significantly raised in cases (p< 0.0005) with {210 (95) IU/L} than the age and sex matched healthy controls {187 (23) IU/L}.

Table 2 Difference in the level of ALP across the Diagnostic Categories (Myocardial Infarction, Complete Heart Block, Chronic Heart Failure and Rheumatic Heart Disease. Two Cases, namely, myocarditis and Congenital Heart Disease were excluded)

(Kruskal-Wallis test)			
	Chi-Square	df	Asymp. Sig.
ALP	1.2	3	0.743

* Significant at 0.05 level.

It is observed from the above table that there is no statistically significant difference in the ALP levels across the diagnostic categories.

DISCUSSION

The main finding of this study was that, in different cardiac diseases (Myocardial Infarction, Chronic Heart Failure, Rheumatic Heart Disease, Complete Heart Block, congenital heart disease and myocarditis) the serum ALP activity was significantly raised compared age and sex matched healthy controls. Also we performed Kruskal-Wallis test to distinguish increased level of serum ALP activity across diagnostic categories. Between different cardiac diseases, there was no significant difference was observed.

The mechanism behind this may be vascular calcification where ALP shown to be a regulator. It was observed that organic pyrophosphate (PPi) inhibits vascular calcification. PPi is hydrolyzed by membrane-bound metallo enzyme ALP in alkaline medium. Thus the role of ALP has been tinted in terms of its effect on vascular diseases (7)(10)(11)(12)(13)(14)(9) where the physiological concentration of PPi inhibits calcium and phosphate deposition completely(10). ALP is fairly ubiquitous in human body which is specifically concentrated in bone, liver, placenta, leukocytes and kidneys. Low level of serum calcium level leads to release of ALP by osteoblastic cells of bone. So it is an important iso-enzyme for bone mineralization(15). Currently, it was suggested that in mineral metabolism ALP plays an important role and might be a molecular marker for vascular calcification(11). Assuming vascular calcification is an important process in atherosclerosis which further leads to vascular hardening and ageing(11)(14). Serum ALP activity levels might have linked with poor vascular outcome in overall patients with Myocardial Infarction, Chronic Heart Failure, Rheumatic Heart Disease, Complete Heart Block, congenital heart disease and myocarditis with deteriorated vascular system.

Harmful effect of serum ALP on clinical outcome can be considered with different methods. As we have measured serum level of tissue non-specific ALP which is measurably concentrated in bone, liver, placenta and kidney. So the confounding factors like liver disease, bone disease patients and pregnant woman are excluded from the study.

Our study goes hand in hand with Kilit Celal (2017) who found significantly increased ALP level in with non—ST-segment elevation myocardial infarction (NSTEMI) (2). Bhavsar *et al* (2015) assessed an significantly increased ALP in CAD patients and suggested to be a significant independent risk factor of CAD(7). Panh *et al* (2017) showed higher ALP levels positively and independently are associated with coronary artery calcification. They suggested that metabolic pathway of

ALP and inorganic pyrophosphate can be a target for new therapies against vascular calcification(10). Park *et al* (2013) confirmed independent association between high ALP and MI(11). Tonelli *et al* (2009) also found an independent association between higher levels of ALP with adverse outcomes among survivors of MI and in a general population sample with larger sample size(12). In conclusion, serum ALP activity is significantly increased in different cardiac diseases, ALP which is routinely measured liver function test which does not need extra cost can be considered as an invaluable marker, not only in existing studies but also in historical and retrospective studies, and studies performed in developing countries. Even though our study indicated ALP as a CVD marker further research is needed with specific isoenzyme study of ALP in large cohorts and diverse ethnic population, so that can be considered in a panel of marker for cardiovascular risk.

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