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Serum Phosphorus level: A marker of myocardial infarction

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Abstract

Introduction: The serum phosphorus level is recently considered as one of the foretelling markers for the severity of cardiovascular diseases. Therefore, this study is aimed to investigate whether the serum phosphorus level in myocardial infarction patients with normal kidney function against healthy individuals could act as a possible marker for identification of vulnerability in cardiovascular diseases.
Method: This is observational case control study of 70 controls and 70 patients who were admitted in ICCU of S.S.G. Hospital, Baroda. Routine parameters, serum Phosphorus & lipid profile, CKMB levels were performed.
Result: Serum Phosphorus, S. HDL and S. LDL showing significant correlation (p-value <0.0001). The study correlates well with the increase in Serum Phosphorus level with decrease in S.HDL and increase in S.LDL.
Conclusion: Serum phosphorus level might be used as similar to lipid profile and/or other risk factors alteration. The serum phosphorus level is recently being considered as one of the foretelling markers for the severity of cardiovascular diseases because of its role in vascular calcification and oxidative stress.
Keywords: Serum Phosphorus, HDL, LDL, Myocardial infarction.

complexes (i.e., aggregates of calcium phosphate and proteins released from remodelling bone that may initiate ectopic mineralization)[2]. Abnormalities in mineral metabolism that enhance the calcium X phosphate product (Ca x P) may further exacerbate vascular calcification initiated by any of these mechanisms. Recent evidence implicates elevated phosphate as a major inductive factor for vascular calcification and osteopontin as an inducible inhibitor of vascular calcification [5].

Elevated serum phosphorus (in the form of phosphate) is a major risk factor for vascular calcification and cardiovascular mortality in ESRD patients [6]. Although elevations in the Ca X P may thermodynamically drive calcification, growing evidence indicates that direct effects of elevated phosphate on vessel wall cells may be more important in regulating the propensity of the vessel to calcify. *In vitro* study, found that heterogeneous, uncloned populations of vascular smooth muscle cells (VSMCs) do not spontaneously mineralize in culture, but can be induced to mineralize by elevating phosphate levels in the culture medium to those typically observed in hyperphosphatemia individuals [6]. Under these conditions, the extracellular matrix surrounding the VSMCs undergoes calcification with features similar to that observed in bone and in pathological vascular calcification *in vivo*, including the presence of calcifying collagen fibres, matrix vesicles, and bio apatite [7].

In rural areas with dearth of good laboratory and healthcare services, it has become difficult to measure these markers. So, serum phosphorus level was estimated along with routine biochemical parameter in patients of myocardial infarction and compared with controls to evaluate if it can be used as simple and cost effective (supportive marker) marker of CAD risk assessment although they cannot be used in isolation as well as not for definitive diagnosis of acute presentation of MI [8].

2. Materials & Methods

It is an observational case control study. It was conducted at SSG Hospital Baroda, 70 diagnosed cases of acute myocardial infarction and 70 healthy subjects within the same age group (as controls)were included in the study of both sexes of age group 30- 65 years.

The Ethical approval has been granted from SSG Hospital & Medical College, Baroda, Gujarat. The procedures followed were in accordance with the ethical standards of the committee on human institutional experimentation and with the Helsinki Declaration of 1975 that was revised in 2000.

2.1 Inclusion criteria

Clinically diagnosed patient with electrocardiographic changes and elevated cardiac biomarkers between 30-65 years of age.

2.2 Exclusion criteria

Patients suffering from diabetes, renal disorders, alcoholics and smoker, along with that patient taking lipid-lowering drugs, diuretics and vitamin supplements were excluded from the study.

2.3 Methodology

Blood samples were analysis in Clinical chemistry laboratory of Dept. of Biochemistry, Baroda Medical College & S.S.G. Hospital, Baroda.

The following blood parameters were analyzed.

Serum Phosphorus: By UV-End point method; Serum Total Cholesterol: Enzymatic colorimetric method; Serum Triglyceride: Enzymatic colorimetric method; LDL Cholesterol: Direct enzymatic method; HDL Cholesterol: Direct enzymatic method; Estimation of VLDL; Serum creatinine: Jaffe's method; Serum Urea: enzymatic method; plasma glucose by GOD- POD method; CK-MB: Modified IFCC immunoinhibition method was measured.

2.4 Statistical analysis

All data analysis was done using Microsoft Excel and the Statistical software MedCalC version 11.5.0. Mean ± Standard deviation calculated. Results were analysed statistically for significance by Independent 't' test and chi square test. And Pearson correlation 'r' test (correlation coefficient test) was done to assess the relation of Serum phosphorus with various lipid profile parameters. Cohen's ES standards were used to calculate the p values, at, p-value <0.05, results were considered significant.

The Gender wise comparison was done in the study. Along with that other clinical parameters were compared in controls and patients. Further, the patients have been divided into two groups depending on serum phosphorus level - Group I (≥ 5 mg/dl) and Group II (≤ 5 mg/dl).

3. Observations

Table 1: Gender wise comparison of subjects in study

Cases	Gender	No.
Patients	Male	51
	Female	19
Control	Male	60
	Female	10

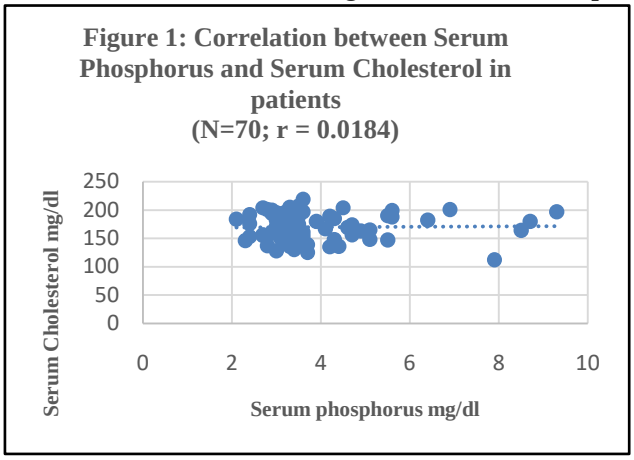
Table 2: Comparison of clinical parameters in controls and patients

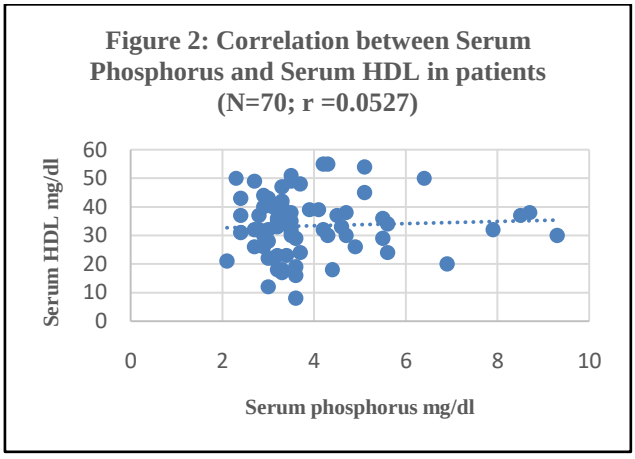
Parameters	Reference range	Controls		Patients		p-Values
		Mean	SD	Mean	SD	
Phosphorus	2.5-4.5 mg/dL	2.7	0.80	3.97	1.51	<0.0001
Total Cholesterol	150-240 mg/dL	169.9	24.4	187.3	40.3	0.0024
HDL	>40 mg/dL	41.0	9.57	33.6	10.6	<0.0001
LDL	<130 mg/dL	108.8	23.4	129.1	30.2	<0.0001
VLDL	<35 mg/dL	20.3	7.37	27.0	16.4	0.0022
TG	<200 mg/dL	119.9	36.9	140.4	69.11	0.0303
RBS	Upto 140 mg/dL	97.6	15	133.3	32.16	<0.0001
Urea	15-45 mg/dL	25.6	6.6	37.2	18	<0.0001
Creatinine	0.6-1.4 mg/dL	0.8	0.2	1.0	0.3	<0.0001

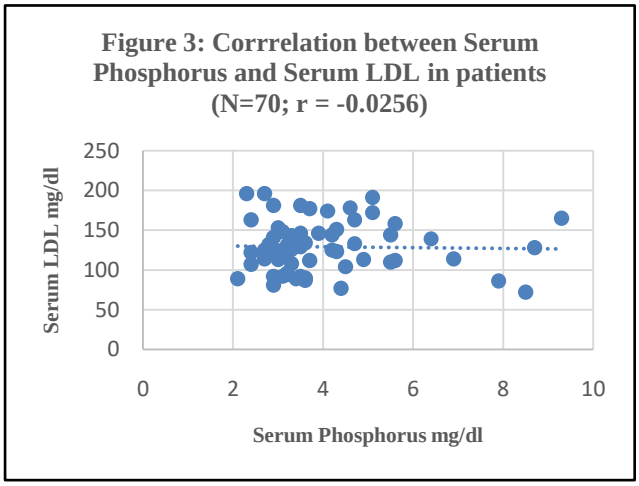
Table 3: Serum Phosphorus levels in AMI subjects

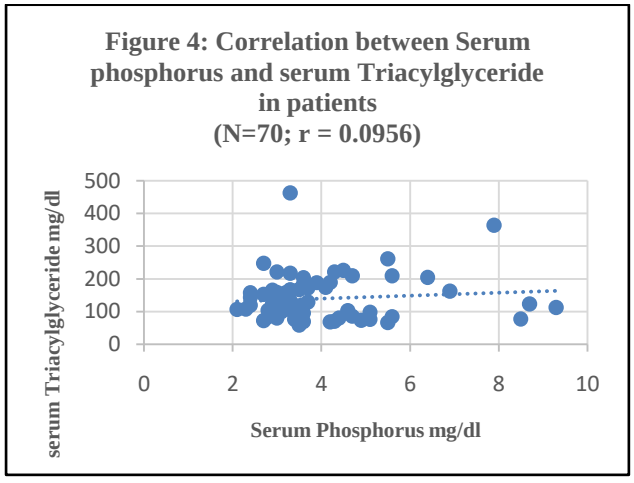
Controls	Patients		p-Values
	Group-I	Group-II	
2.7±0.80 mg/dl	5.48±1.98 mg/dl*	2.46±1.68 mg/dl	<0.0001*
Total no of patients	20/70	50/70	-
Mortality	4/20 (20%)	1/50 (2%)	<0.001*
***Indicates level of significance with Grp I Paired T Test Analysis was done for p Value**			

Figures: Correlation of parameters with Serum Phosphorus









In the above shown figures, the serum cholesterol, serum HDL, and Serum TG are showing mild positive correlation with the serum phosphorus. While Serum LDL is showing mild negative correlation with the serum phosphorus.

4. Results

The Comparison of clinical parameters in controls and patients, where Serum Phosphorus, Serum HDL and Serum LDL parameters have shown significant level of changes.

Serum Phosphorus, S. HDL and S.LDL showing significant result (p-value <0.0001). This study correlates well with the increase in S. Phosphorus level with decrease in S.HDL and increase in S.LDL which is one of the factors causing MI in patients. Hyperphosphatemia was observed in (29%), of AMI patients 20/70 these patients formed group I of the study, rest (71%) patients 50/70 with normal phosphate levels formed group II.

The Pearson's correlation 'r' test (correlation coefficient test) was done to assess the relation of Serum phosphorus with various lipid profile parameters, where Serum phosphorus is showing mild correlation with Serum Cholesterol, Serum HDL and Serum TG and mild negative correlation with Serum LDL.

5. Discussion

This study was conducted to document the serum Phosphorus levels in patients with MI, whether there is any correlation. The result of this study showed that the studied variables (Serum Phosphorus, Serum HDL, Serum LDL) were significant in the studied group (p- value <0.0001), while Serum TG is showing mild correlation.

It has been suggested from various clinical studies, an elevated level of serum phosphorus load is positively correlated with mortality. It also acts as an inducer in vascular complication with an increase risk in progression to death [9,10].

The burden of causing vascular disease in known population having abnormalities in Ca & PO_4 metabolism with abnormal renal function is directly related. In patients without CKD, vascular calcification has been observed as a result of the atherosclerosis and not as a primary calcifying process in vessels.

In patients with normal renal function, recently some studies have shown that higher phosphate levels even within the normal range are associated with abnormal vascular phenotypes. The outcome composite of MI, stroke, TIA, heart failure as a CVD event that is due to increased carotid intima- medial stiffness and arterial stiffness. The effect of phosphorus (Pi) on calcification of human smooth muscle cell (HSMC) examined in vitro cell culture model [8]. It has been proved that cell cultures are susceptible to calcification when cultured in media containing pi levels resembling those usually found in patients with hyperphosphatemia[10]. The hypothesis has been supported by these results along with observations from other studies that vascular smooth muscle cells (VSMCs) increase phosphate uptake via a type III sodium dependent phosphate cotransporter (NPC[pit-I]) is induce directly by elevated phosphorus level. Increased intracellular phosphate serves as a signal for osteogenic gene expression (cbfa-I and downstream targets osteopontin and osteocalcin) and as a suppressor of HSMC-specific gene expression, resulting in increased secretion of mineral-nucleating molecules (matrix vesicles, calcium-binding proteins and collagen-rich extracellular matrix). These factors combine to transform the cell to be susceptible to vascular calcification [6]. A clear link between phosphate induced calcification and oxidative stress of mitochondria, activation of nuclear factor-kβ and subsequent increase in expression of osteogenic factors resulting in vascular mineralization was recently demonstrated by Zoo *et al*[11,12]. The study was conducted at Govt. Hospital most of the patients are from lower socio-economic strata and BPL level; therefore, many factors could not be taken into consideration. Thus, the study has its own limitations.

6. Conclusion

Serum phosphorus may be added as a possible marker for the diagnosis of the risk of similarity to lipid profile and/or other risk factors and it is showing correlation with lipid profile parameters, because of its role in vascular calcification and oxidative stress.

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Conflict of interest: - Nil