



ISSN: 0975-833X

Available online at <http://www.journalcra.com>

International Journal of Current Research
Vol. 9, Issue, 12, pp.62979-62981, December, 2017

INTERNATIONAL JOURNAL
OF CURRENT RESEARCH

RESEARCH ARTICLE

CHANGES IN SERUM ALBUMIN AND PHOSPHORUS LEVELS ARE CLOSELY RELATED TO INCREASED RISK OF CORONARY ARTERY DISEASE

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ARTICLE INFO

Article History:

Received 12th September, 2017

Received in revised form

09th October, 2017

Accepted 20th November, 2017

Published online 27th December, 2017

Key words:

CAD, Albumin,
Phosphorus,
CRP.

ABSTRACT

Introduction: Hypoalbuminemia and hyperphosphatemia are associated with increased morbidity and mortality associated with cardiovascular disease. Albumin behaves as an antioxidant molecule whereas increased serum phosphorus levels are linked with vascular calcification.

Method: Present study is a case-control study. Hundred CAD patients were recruited adopting an inclusion and exclusion criteria. 100 age and sex matched healthy subjects were taken as controls. CAD patients were segregated into two Groups on the basis of their albumin cut off value of 4.0g/dl. All the subjects were screened for serum albumin, A/G ratio, quantitative CRP and serum phosphorus levels. Data was statically analysed.

Results: CAD patients had significantly low ($p < 0.05$) serum albumin, A/G ratio and high CRP and serum phosphorus levels as compared to healthy controls. On further segregation, Group 1 CAD patients having albumin levels less than 4.0g/dl were observed to have significantly raised ($p < 0.05$) serum CRP and phosphorus levels together with markedly low A/G ratio as compared to Group 2 CAD patients.

Conclusion: hypoalbuminemia and hyperphosphatemia further aggravates the oxidative stress present in CAD patients. It is advocated that changes in serum albumin and phosphorus should be monitored in CAD patients during diagnosis as well as during prognosis.

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Citation: Ritu Sharma, Sheetal Pahwa, Balwant Singh and Singh, H.P. 2017. "Changes in serum albumin and phosphorus levels are closely related to increased risk of coronary artery disease", *International Journal of Current Research*, 9, (12), 62979-62981.

INTRODUCTION

Albumin plays a vital role in metabolic reaction in human body. Its role in coronary heart disease was documented in 1989 where it was shown that there was marked increase in cardiovascular disease mortality with decreasing albumin levels among males in the British Regional Heart Study (Phillips *et al.*, 1989). However, the workers described their results as serendipitous because of lack of prior hypothesis. But Subsequent studies reported increased risk of CAD in subjects having relatively low serum albumin levels as compared to those having high levels (Corti *et al.*, 1996, Gillum and Makuc; 1992, Nelson *et al.*, 2000). Low serum albumin concentration have been associated with increased inflammation, increased blood viscosity and disturbed endothelial function (Joles *et al.*, 1997). Human serum albumin contains one free cysteine derived redox reactive thiol group which confers antioxidant potential to it.

During oxidative stress synthesis of albumin by the liver gets switched to other acute phase proteins such as CRP. Hence, it is important to study variations in both these parameters under diseased conditions. In addition to albumin, another important molecule which plays a key role in vascular calcification is phosphorus. Phosphorus homeostasis has been reported to be disturbed in CAD patients (Robert *et al.*, 2009). It has been reported that hyperphosphatemia induces vascular smooth muscle cell transformation into osteoblast like cells leading to calcification (Chen *et al.*, 2002). Also phosphorus rich environment produces high levels of ROS and less nitric oxide in bovine aortic endothelial cells. It is evident that CAD is associated with increased prevalence of oxidative stress and adverse changes in mineral metabolism. Hence, the present study was aimed to understand the variations in serum albumin and its relationship with changes in CRP, Albumin/Globulin (A/G) ratio and serum phosphorus in Coronary artery disease patients.

MATERIAL AND METHODS

The present study was conducted in the Department of Biochemistry at Govt. Medical College Amritsar, Punjab. 100

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diagnosed cases of CAD were taken from the Out Patient Department of the private hospital at Amritsar. CAD patients were divided into two Groups on the basis of the Albumin cut off value of 4g/dl (selected in the present study)

Group 1: This group comprised of CAD patients having serum albumin levels <4g/dl

Group 2: This group comprised of CAD patients having serum albumin levels >4g/dl

Exclusion criteria: Diabetic patients, patients having major renal complications, lung disease, liver disease, thyroid disorder, gout, acute infections, smokers and chronic alcoholics were excluded from the study. 100 age and sex matched healthy subjects were taken as controls from the general population. Written informed consent was obtained from all the subjects. 5 ml venous blood sample was obtained under sterilized conditions. Serum was separated for the following investigations:

Serum albumin was estimated with the End point BCG dye method, CRP levels by quantitative turbidimetric immunoassay, serum phosphorus was estimated by Daly and Ertingshausen's method.

Statistical Analysis: Data was statistically analyzed. Student t test was applied and significance was tested at $p < 0.05$.

RESULTS

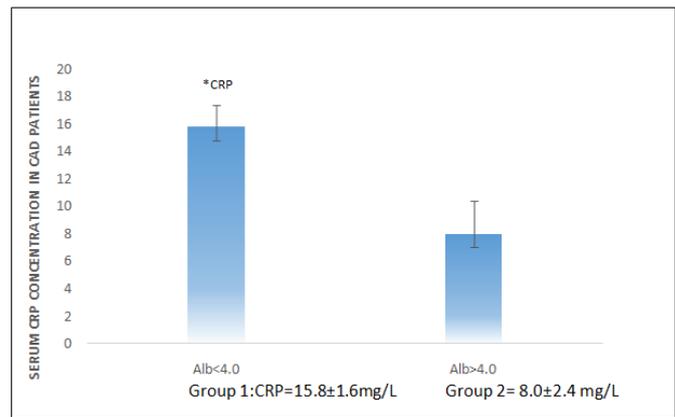
Serum albumin levels were significantly low ($p < 0.05$) in CAD patients as compared to controls while serum phosphorus levels were significantly high together with raised serum CRP levels (Table 1).

Table 1. Variations in serum Albumin, phosphorus and CRP levels in CAD patients as compared to controls

Parameters Subjects	Serum Albumin(g/dl)	Serum phosphorus (mg/dl)	Serum CRP (mg/L)
Controls (n=100)	5.2±1.4	2.8±1.0	3.4±2.4
CAD patients (n=100)	3.1±0.9*	5.5±1.6*	15±2.4*

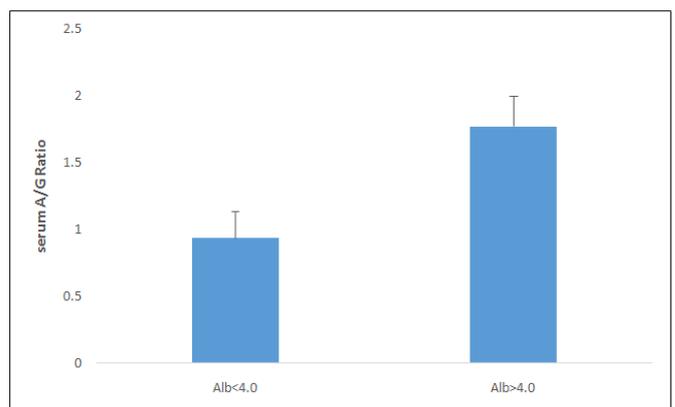
* $p < 0.05$; Results are expressed as Mean±S.D.

Fig 1 shows variations in serum CRP levels in CAD patients having serum albumin less than 4g/dl (Group 1) as compared to those having levels more than 4g/dl (Group 2). Serum CRP levels were significantly raised ($p < 0.03$) in Group 1 CAD patients having serum albumin concentrations less than 4g/dl as compared to Group 2 CAD patients. However, overall CRP levels (8 ± 2.6 mg/L) in CAD patients having albumin levels more than 4g/dl were relatively high as compared to controls (3.4 ± 2.4 mg/L; Table 1). Fig 2 shows variations in serum A/G Ratio in Group 1 and Group 2 CAD patients. Serum A/G ratio was significantly low ($p < 0.05$) in CAD patients having albumin concentration less than 4 g/dl as compared to those with serum albumin levels more than 4.0g/dl. This clearly indicates the prevalence of inflammation and increased oxidative stress associated with hypoalbuminemia. Fig 3 shows variations in serum phosphorus levels in Group 1 and Group 2 CAD patients. Group 1 CAD patients having albumin levels less than 4g/dl were observed to have significantly high serum phosphorus levels as compared to Group 2 CAD patients.



Data is expressed as Mean±S.E.; * $p < 0.05$

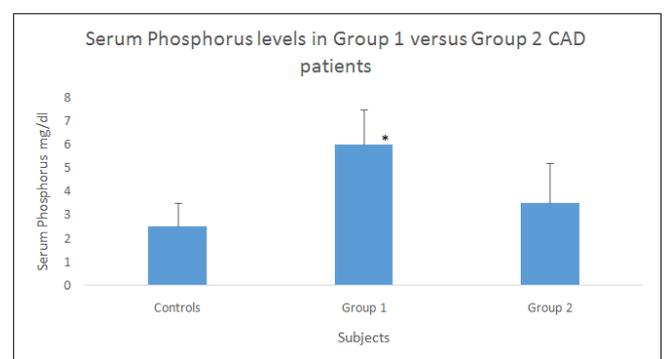
Fig. 1. Raised Serum CRP levels in CAD patients with albumin concentration <4.0 g/DL



Results are expressed as Mean±S.E. Mean A/G Ratio in Group 1 CAD patients was 0.93 ± 0.54 and in Group 2 CAD patients was 1.77 ± 0.64 ; $p < 0.05$

Fig. 2. Variations in serum A/G ratio in Group 1 and Group 2 CAD patients

Overall serum phosphorus levels were significantly high in CAD patients as compared to controls.



Results were expressed as Mean±S.E. mg/dl; Serum phosphorus levels in controls were 2.5 ± 1.0 mg/dl; Group 1= 6 ± 1.5 mg/dl; Group 2= 3.5 ± 1.7 mg/dl; * $p < 0.05$

Fig. 3. Variations in serum phosphorus levels in Group 1 and Group 2 CAD patients

DISCUSSION

Coronary artery disease is a state of marked oxidative stress and inflammation. Serum albumin is a negative acute phase reactant that is synthesized in liver. During oxidative stress, enhanced activity of macrophages and other cells of immune system lead to overproduction of cytokines which switch

albumin synthesis to other acute phase proteins such as CRP (Kushner; 1982). This clearly show how important is to maintain the albumin levels in human body. In the present study, we tried to study the variations in serum albumin levels in CAD patients as compared to healthy controls. Also, it was attempted to evaluate variations in serum CRP, A/G Ratio and phosphorus in CAD patients who were segregated into two groups on the basis of albumin cut off value of 4.0g/dl. CAD patients were observed to have significantly low serum albumin levels and raised CRP and phosphorus levels as compared to controls. Albumin is such a vital molecule that its deficiency due to any disease may affect the metabolism to an alarming extent. Number of studies reported the association of low serum albumin with increased cardiovascular morbidity and mortality (Luc Djousse *et al.*, 2002, Celik *et al.*, 2016). This is because hypoalbuminemia is linked to fibrinolysis, hypertension, increased vascular permeability and platelet aggregation. All these factors enhance CAD risk. Furthermore, variations in serum albumin levels lead to switch in its synthesis to other acute phase proteins such as CRP. Consequently, increase in CRP levels may be associated with low serum albumin levels. This was observed in the present study. CAD patients having albumin levels less than 4g/dl (Group 1) had relatively more raised levels of CRP than those having levels more than 4.0g/dl (Group2). Also Group 1 CAD patients had significantly low A/G ratio as compared to Group 2 CAD patients. This is indicative of marked oxidative stress and inflammation in patients with relatively low serum albumin levels.

Another interesting finding was that CAD patients had significantly raised serum phosphorus levels than controls. Group 1 CAD patients had more raised serum phosphorus levels than Group 2 CAD patients. Experimental evidence has shown that exposure of animals to higher phosphorus results in expression of osteogenic phenotype in vascular smooth muscle cells causing vascular calcification. Other potential mechanisms linking hyperphosphatemia with CAD are inhibition of vitamin D synthesis and increased PTH levels (Zittermann *et al.*, 2003). Studies have reported raised serum phosphorus levels in CAD patients with or without kidney disease (Mahmud *et al.*, 2011, Chonchol *et al.*, 2009). The results from the present study clearly indicate that hypoalbuminemia is a potential trigger for aggravating oxidative stress. Raised serum phosphorus levels may add to further complications because of its strong association with atherogenic factors. Hence it is advocated to give special attention to serum albumin and phosphorus levels while monitoring CAD patients in order to control the advanced complications.

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