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RESEARCH ARTICLE

STUDY OF SERUM PHOSPHATE AND ALBUMIN LEVELS AND THEIR ASSOCIATION WITH COMPONENTS OF METABOLIC SYNDROME

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ABSTRACT

Introduction: Metabolic Syndrome represents a cluster of cardiovascular risk factors that recently has become a public health problem. It has been proposed that disturbances in phosphate metabolism may contribute to the development of this constellation of cardiovascular risk factors. Lower serum albumin was regarded as an indicator of malnutrition, inflammation, and liver disease, and has been reported to be associated with increased cardiovascular morbidity and mortality.

Aim: To determine the association between serum phosphate and albumin levels with the components of metabolic syndrome.

Method: A case- control study was carried out with hundred subjects. Fifty of these subjects were diagnosed with metabolic syndrome according to National Cholesterol Education Program Adult Treatment Panel III, while other fifty were sex and age matched healthy control subjects.

Results: The mean serum phosphate level is 2.8±0.65mg/dl in cases and 3.4±0.76 mg/dl for controls. All patients with metabolic syndrome showed low phosphate levels with $p<0.001$ compared with controls. The mean serum albumin level is 3.1±0.74g/dl in cases and 3.67±0.82g/dl for controls. Patients with metabolic syndrome showed significantly low albumin levels with $p<0.001$ compared to controls.

Conclusion: The results of this study indicate that patients with metabolic syndrome had significantly lower phosphate and albumin concentrations compared to individuals who do not fulfill criteria for the diagnosis of this syndrome. This reduction in serum phosphate and albumin levels is more pronounced as the number of components of metabolic syndrome increases.

INTRODUCTION

In India, prevalence of metabolic syndrome is predicted to be 26.6% and 2.6 million and Indians are predicted to die due to Cardiovascular Diseases (CVD) by the year 2020 Reddy *et al.* (2006). Metabolic syndrome consists of a constellation of metabolic abnormalities that confer increased risk of cardiovascular disease and diabetes mellitus Robert H Eckel, (2008). Despite important recent advances in the understanding of the consequences of metabolic syndrome, its pathophysiological characteristics remain unclear. It has been proposed that disturbances in phosphate metabolism may contribute to the development of this constellation of cardiovascular risk factors. Similarly, regarding serum albumin some observational studies have linked higher Serum albumin levels to cardiovascular risk factor including blood pressure and cholesterol Kalaitzidis *et al.* (2005). In addition to this some studies have reported lower serum albumin in malnutrition, inflammation and also with increased CVD morbidity and mortality Phillips *et al*. (1989). The aim of this study was to determine the association between serum phosphate and albumin levels with the components of metabolic syndrome. Informed oral consent was obtained from all the study participants. The ethical committee of our college has approved this study.

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MATERIALS AND METHODS

Study was conducted on patients with metabolic syndrome attending the outpatient & in patient departments of Medicine in Victoria hospital and Bowring and Lady Curzon Hospitals attached to Bangalore Medical College and Research Institute, Bangalore. Sample size was total of 100 subjects, with 50 cases and 50 age and sex matched controls. All patients were diagnosed according to National Cholesterol Education Program, Adult Treatment Panel III criteria and it requires the presence of 3 or more of the following (NCEP 2002): a. Fasting blood glucose ≥110 mg/dl b. Serum triglyceride ≥150mg/dl or being on lipid lowering therapy c. Serum HDL <40 mg/dl in men and <50 mg/dl in women or being on antilipidemic therapy d. Blood pressure ≥130 mmHg systolic and ≥85 mmHg diastolic or being on antihypertensive therapy and e. Waist circumference >102 cm in men and >88 cm in

women. Patients with following history were excluded: a. Alcohol intake more than 30 g/day (≈ 38 ml of 100% alcohol) and patients with smoking history b. Patients with known preexisting liver or kidney diseases c. Use of hepatotoxic drugs and d. Acute infectious/inflammatory conditions. Venous blood samples of about 5 ml were obtained in the morning after an overnight fast by venepuncture under aseptic precautions. After centrifugation, serum was used for estimation of parameters required for the study. Estimation of serum phosphate was by Fiske and Subbarow method. Estimation of serum Albumin was by Bromo Cresol Green method. Serum phosphate and albumin levels were analyzed by Beckman Coulter AU 480 auto analyzer using standard kits. Other parameters studied were fasting lipid profile by enzymatic method, Fasting blood sugar were hexokinase method, Liver function tests by enzymatic and colorimetric method, serum creatinine by jaffe kinetic method. Body Mass Index Waist circumference was measured midway between the last rib and iliac crest. Body mass index expressed as Kg/m^2.

Statistical Analysis

Metabolic syndrome cases and controls were grouped according to NCEP ATP III criteria.

Study design: A case control study with 50 cases and 50 controls were undertaken to study serum phosphate and serum albumin levels and their association with components of metabolic syndrome.

Statistical Methods: Descriptive statistical analysis has been carried out in the present study. Results on continuous measurements are presented on Mean ± SD (Min-Max) and results on categorical measurements are presented in Number (%). Chi-square/ Fisher Exact test has been used to find the significance of study parameters on categorical scale between two or more groups.

Statistical software: The Statistical software namely SAS 9.2, SPSS 15.0, Stata 10.1, Systat 12.0 and R environment ver.2.11.1 were used for the analysis of the data and Microsoft word and Excel have been used to generate graphs, tables etc.

Table 1. Clinical characteristics of the study population

	Controls	Metabolic syndrome	p
No of subjects	50	50	
Sex (male/female)	18/32	20/30	NS
age	50.2 ± 9	51.4 ± 9.7	NS
BMI (kg/m^2)	21.5 ± 3.5	29.6 ± 3.9	<0.0001**
Waist circumference (cm)	92.5 ± 10.3	104 ± 9.5	<0.0001**

NS- Not significant
+ Suggestive significance (P value: 0.05<P<0.10)
* Moderately significant (P value:0.01<P ≤ 0.05)
** Strongly significant (P value : P≤0.01)

Table 2. Biochemical characteristics of the study population

Biochemical Characteristics of the Study Population

VARIABLES	CONTROLS	METABOLIC SYNDROME	p VALUE
Glucose (mg/dL)	73.8 ± 16.8	116.8 ± 37.6	<0.0001***
Total cholesterol (mg/dL)	149 ± 45.2	169.5 ±53.4	<0.05*
Triglycerides (mg/dL)	127 ± 77.8	164.9 ± 85.3	<0.05*
HDL cholesterol (mg/dL)	37.1 ± 11.2	28.4 ± 10.4	<0.05*
Serum albumin (mg/dL)	**3.67 ± 0.82**	**3.18 ± 0.74**	**<0.01****
Aspartate aminotransferase (IU/L)	19.8 ± 7.9	24.26 ± 15	0.06
Alanine aminotransferase (IU/L)	17± 9.7	22.38 ± 12.1	<0.01**
Alkaline Phosphatase (U/L)	71.4 ± 25.6	83.5 ± 33.9	< 0.05*
Serum phosphate (mg/dL)	**3.4 ± 0.76**	**2.8 ± 0.65**	**< 0.001*****
Serum creatinine (mg/dl)	0.7 ±0.3	0.61 ± 0.3	<0.01**

NS- Not significant
+ Suggestive significance (P value: 0.05<P<0.10)
* Moderately significant (P value:0.01<P ≤ 0.05)
** Strongly significant (P value : P≤0.01)

This graph shows the distribution of phosphate levels after study participants were classified according to their total number of components of metabolic syndrome (Figure 1). As shown, there was a strong decrease in phosphate values as the number of components of metabolic syndrome increased (P < 0.01**).

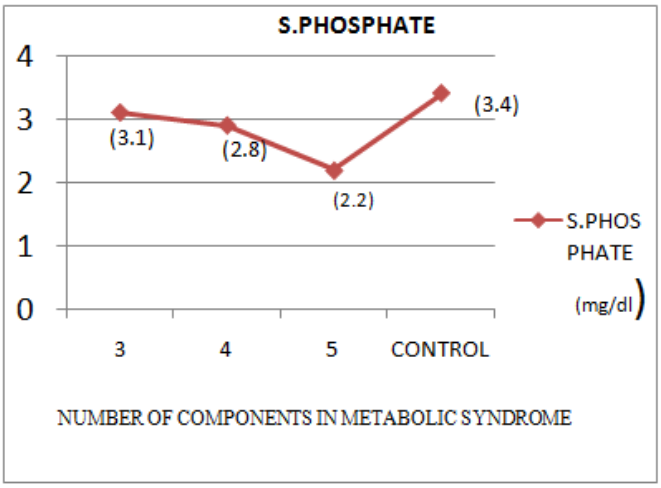

Figure 1. Distribution of S.Phosphate based on number of components in Metabolic syndrome

This graph shows the distribution of s.albumin levels after study participants were classified according to their total number of components of metabolic syndrome (Figure 2). As shown, there was a significant decrease in albumin values as the number of components of metabolic syndrome increased (P < 0.01**).

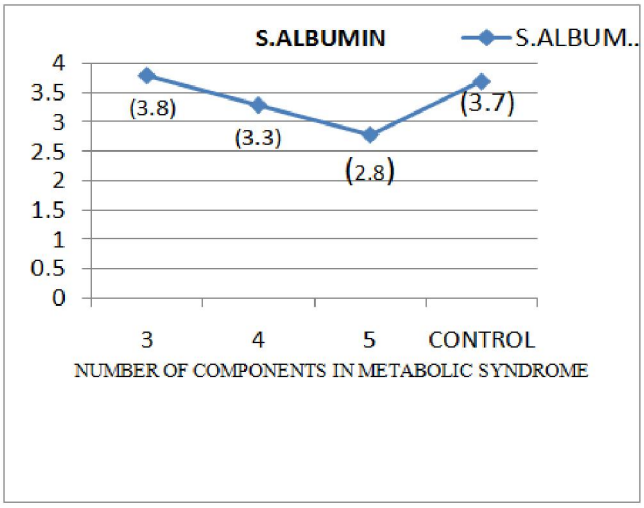

Figure 2. Distribution of S. Albumin based on number of components in metabolic syndrome

DISCUSSION

The metabolic syndrome comprises a cluster of cardiometabolic risk markers with insulin resistance and adiposity as central features Robert H Eckel (2008). It has been hypothesized that a state of chronic low-grade inflammation associated with excess adipose tissue may explain the development of the obesity related pathologies, such as type 2 diabetes mellitus and cardiovascular disease Hotamisligil (2006). Previous studies have shown that obese and hypertensive subjects had significantly lower phosphate levels compared with healthy individuals Park *et al.* (2009). Our study has also showed significantly lower phosphate concentrations compared with controls, Serum Phosphate is involved directly in carbohydrate metabolism; hypophosphatemia can result in impaired utilization of glucose, insulin resistance, and hyperinsulinemia Paula *et al*. (1998). Study by Hagelin L proposed causal relationship between low serum phosphate and the clustering of risk factors is based on results from a cross-sectional study of obese patients, where low serum phosphate was associated with high body mass index (BMI), high blood glucose, high blood pressure, but low serum high density lipoprotein Haglin (2009). According to Rigas Kalaitzidis *et al.* conducted a cross sectional study that showed patients with metabolic syndrome had significantly lower phosphate levels (3.0± 0.5) compared with healthy individuals(3.3 ± 0.5),which is considered significant(p<0.001) Kalaitzidis *et al.* (2005). Wan Park *et al*. studied 46,798 subjects over 20 years. The median plasma phosphate level was 3.49 ± 0.44 mg/dL and it was found that serum phosphate levels had a positive correlation with total cholesterol, HDL-C, lipoprotein a, apolipoprotein A1, calcium, and albumin Park (2009). In addition, serum phosphate levels had a negative correlation with age, body mass index, uric acid, fasting glucose, insulin, HOMA-IR, HS-CRP, triglyceride levels, systolic blood pressure, diastolic blood pressure, and waist circumference ($P < 0.001$).

Hence, hypophosphatemia in patients with metabolic syndrome can be attributed to decreased dietary intake, as well as internal redistribution of this element. Serum albumin level is a marker of nutritive conditions, acts as an antioxidant, and is a plasma volume expander (Harris and Haboubi 2005; Roche *et al.,* 2008). It is reduced in various diseased conditions, involving malnutrition and inflammation Phillips *et al.* (1989). Low serum albumin levels attribute to risk of developing stroke and coronary heart disease. This study finding was consistent with the study by Phillips et al who reported a strong association between serum albumin and cardiovascular mortality, which persisted after controlling serum total cholesterol and six other risk factors, not including high density lipoprotein (HDL) cholesterol Haglin (2009). In the Framingham Offspring Study, conducted in the year 2002, people with lower serum albumin levels had unfavorable cardiovascular risk profiles, such as higher BMI, total cholesterol, cigarette smoking, and lower HDL cholesterol Djousse *et al.* (2002). Our study results suggest that low albumin levels might be a reflection of the chronic inflammatory process rather than an independent risk factor of cardiovascular disease in metabolic syndrome. Follow-up studies are merited to investigate the serum albumin levels as a prospective risk factor of metabolic syndrome.

Conclusion

In conclusion, patients with metabolic syndrome show significantly lower phosphate and albumin concentrations compared with individuals who do not fulfill criteria for the diagnosis of this syndrome. This reduction is more pronounced as the number of components of metabolic syndrome increases. The clinical significance of these disturbances, as well as their importance as targets for preventive or therapeutic interventions, remains to be established.

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