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MODIFIED METABOLIC SYNDROME

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ABSTRACT

BACKGROUND: Metabolic syndrome refers to a set of clinical factors leading to a multitude of complex multi-system complications. Derangement of phosphate homeostasis may suggest a tendency towards metabolic syndrome. **OBJECTIVE:** To determine the frequency of hypophosphatemia in patients with metabolic syndrome **METHODOLOGY:** A cross-sectional study undergone from February to August 2024 upon a sample of 150 consenting adults of either gender, diagnosed with Metabolic syndrome lasting ≥ 6- weeks duration having age 30-60 years presenting at Liaquat University Hospital, Hyderabad, Pakistan. Data was composed on predesigned proforma and the frequency (percentage) and mean ± SD was calculated for qualitative and quantitative variables. **RESULTS:**, Of the study sample, hypophosphatemia was noted in 90 (60%) patients, from which 49 (54.4%) were males and rest were females .The statistical significance was analyzed for hypophosphatemia in accordance with age (p=0.00), residence (p=0.00), duration of metabolic syndrome, (p=0.03), smoking (p=0.02), obesity (p=0.03), hyperlipidemia (p=0.02), hypomagnesemia (p=0.00), hyperuricemia (p=0.00) and uncontrolled diabetes mellitus (p=0.00) while in context to gender it was observed as non-significant (p=0.13).**CONCLUSION:** There was a significant association of hypophosphatemia among patients with metabolic syndrome, with significant association with regards to various patient demographic and clinical data.

KEYWORDS: Metabolic syndrome, Phosphate, Hypophosphatemia

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INTRODUCTION

Metabolic syndrome (Syndrome X, insulin resistance) has been globally known to be an ongoing public health problem. The Metabolic syndrome is a set of clinical features that are secondary to insulin insensitivity and fatty tissue malfunction. This may include high blood pressures, raised serum glucose and triglycerides, low high density lipoproteins, and truncal obesity.[1-4] Patients who have positive indications of above conditions eventually develop substantial clinical complications,

particularly diabetes mellitus and cardiovascular disease, with a higher chance of cerebral vascular events, fatty liver disease, and malignancy. Numerous associated complications exist such as cardiac failure atrial fibrillation, valvular stenosis and thrombotic phenomenon.[5-6] The reported prevalence of patients with metabolic syndrome with hypophosphatemia is 46%.[1] Phosphorus has important role in carbohydrate processing and its deficiency directly affects glucose consumption, insulin insensitivity, and hyperinsulinemia predisposing to metabolic syndrome.[7] most patients with hypophosphatemia are asymptomatic. Lethargy, bony pain, rhabdomyolysis, and altered mentation may be noted in symptomatic cases. [8]

METABOLIC SYNDROME:

Metabolic syndrome can be labelled when a patient has at least three of the following five conditions: (1) Fasting glucose ≥100 mg/dL (2) Blood pressure ≥130/85 mm Hg (3) Serum Triglycerides ≥150 mg/dL (4) HDL-C < 40 mg/dL in men or < 50 mg/dL in women, (5) Waist circumference ≥102 cm (40 in) in men or ≥88 cm (35 in) in women.[9]

HYPOPHOSPHATEMIA:

Hypophosphatemia was labelled as a serum phosphate level < 2.5 mg/dL. **EFFECT MODIFIERS** were identified and analyzed via stratification after data collection, namely: (1) Smoking**:** ≥5 cigarettes per day for ≥3-year duration (2) Obesity: A body mass index (BMI) ≥27.5 kg/m^2 measured by calculating weight (in kg) over square of height (in meters) (3) Hyperlipidemia: Unusually higher values of any one or all lipoproteins [cholesterol (≥ 200 mg/dl) or low-density lipoprotein (≥100 mg/dl) for at least 14 hours fasting state] (4) Hypomagnesemia: Serum magnesium level ≤2.0 mg/dL (5) Hyperuricemia: Serum uric acid level >6.0 mg/dL (6) Uncontrolled Diabetes Mellitus: Hemoglobin A1c (HBA1c) greater than 6.5%.

MATERIAL AND METHODS

A hospital-based, cross sectional descriptive study was done, over a six-month period from 13 February 2024 to 12 June 2024 in Department of Medicine, Liaquat University Hospital, Hyderabad/Jamshoro. Non-probability consecutive sampling was utilized for sample collection. Following informed consent, the data was noted on pre-determined proforma. Inclusion criteria were: Patients of both genders, between age 30 to 60 years, diagnosed with Metabolic Syndrome for ≥6 weeks' duration. Exclusion criteria were patients with known liver/kidney/thyroid dysfunction, pregnant women, patients with history of alcoholism or drugs history that cross-interact with metabolism of lipids or carbohydrates (corticosteroids, beta-blockers, hormonal replacement therapy, selective estrogen receptor modulators, bisphosphonates, antacids, diuretics, beta- blockers, non-steroidal anti-inflammatory drugs, angiotensin-converting enzyme inhibitors angiotensin II receptor blockers, aminoglycosides), those with malignancy (lung, bone or breast), already on medications of cancer chemotherapy or on phosphate supplements that might affect the phosphate level. The demographic characteristics of the patients and laboratory investigations including Fasting Blood Sugar, HbA1c, complete blood counts, prothrombin time, serum albumin, bilirubin, serum creatinine were obtained. Presence of Diabetes mellitus was confirmed via Fasting blood sugar and HbA1c. The composed dataset was entered in SPSS (version 17.0) and analyzed accordingly. The frequency and % were calculated for gender, smoking, obesity, hyperlipidemia, un-controlled diabetic mellitus, residence (urban and rural), hypomagnesemia, hyperuricemia and hypophosphatemia. The mean and standard deviation

(SD) were calculated for quantitative variables such as age, duration of metabolic syndrome & hemoglobin A1C (HBA1c), BMI and serum phosphate

level. The stratification was done for age, duration of disease, gender, smoking, obesity, hyperlipidemia, un-controlled diabetic mellitus, residence (urban and rural), hypomagnesemia and hyperuricemia to adjust for confounding. The post stratification chi-square test was applied on categorical variables at 95% confidence interval and the p- value ≤0.05 was considered as statistically significant. The blood pressure was measured by sphygmomanometer at least three readings 2 hours apart while the fasting blood sugar and lipid profile was done during fasting state at least 14 hours fasting whereas the waist circumference was measured by estimating abdominal girth via inch tape in standing position and the BMI was also calculated simultaneously through height pointer weight machine. The hypophosphatemia was labeled as per operational definition while the effect modifiers as smoking, obesity, hyperlipidemia, hypomagnesemia, hyperuricemia and uncontrolled diabetes mellitus were also explored.

RESULTS

A total of 150 cases were enlisted in this study. Of these, 59.3%(n=89) were male whereas 40.7% (n=61) were female. 60%(n-90) of study sample had hypophosphatemia whereas 40% (n=6600) did not. There was a statistically significant association observed with hypophosphatemia in association with age (p=0.00), residence (p=0.00), duration of metabolic syndrome, (p=0.03), smoking (p=0.02), obesity (p=0.03), hyperlipidemia (p=0.02), hypomagnesemia (p=0.00), hyperuricemia (p=0.00) and uncontrolled diabetes mellitus (p=0.00) while the in context to gender it was observed as non-significant (p=0.13) respectively

Table 1: Summarized demographic and clinico-laboratorical parameters of study population (n=150)

Variable	Hypophosphatemia		Total	P-value
	Yes	No		
Age				
30-40 years	43(47.8%)	10(16.7%)	53 (35.3%)	0.00
41-50 years	39(43.3%)	42(70.0%)	81 (54.0%)	
51-60 years	8(8.9%)	8(13.3%)	16 (10.7%)	
Gender				
Male	49(54.4%)	40(66.7%)	89 (59.3%)	0.13
Female	41(45.6%)	20(33.3%)	61 (40.7%)	
Residence				
Rural	41(45.6%)	44(73.3%)	65 (43.3%)	0.00
Urban	49(54.4%)	16(26.7%)	85 (56.7%)	
Duration				
6-8 weeks	32(35.6%)	10(16.7%)	42 (28.0%)	
8-12 weeks	30(33.3%)	23(38.3%)	53 (35.3%)	0.03
>12 weeks	28(31.1%)	27(45.0%)	55 (36.7%)	
Smoking				
Yes	56(62.2%)	26(43.3%)	82 (54.7%)	0.02
No	34(7.8%)	34(56.7%)	68 (45.3%)	

Obesity				
Yes	62(68.9%)	31(51.7%)	93 (62.0%)	0.03
No	28(31.1%)	29(48.3%)	57 (38.0%)	
Hyperlipidemia				
Yes	60(66.7%)	29(48.3%)	89 (59.3%)	0.02
No	30(33.3%)	31(51.7%)	61 (40.7%)	
Hypomagnesemia				
Yes	43(47.8%)	43(71.7%)	86 (57.3%)	0.00
No	47(52.2%)	17(28.3%)	64 (42.7%)	
Hyperuricemia				
Yes	67(74.4%)	29(48.3%)	96 (64.0%)	0.00
No	23(25.6%)	31(51.7%)	54 (36.0%)	
Uncontrolled DM				
Yes	73(81.1%)	14(23.3%)	87 (58.0%)	0.00
No	17(18.9%)	46(76.7%)	63 (42.0%)	

DISCUSSION

Prior research has suggested that hypertensive patients with high BMIs in obese category tend to have low phosphorous values as opposed to healthy controls, alongside 8-9 metabolic syndrome. In present study additional clinical data for phosphate metabolism abnormalities in patients with metabolic syndrome and shown significantly lower phosphate concentrations and this reduction was proportional to the metabolic syndrome. Hypophosphatemia may be secondary to reduced intake in diet, decreased gut absorption, increased renal losses or internal redistribution.[2] In 2001, Haglin L, proposed that an unbalanced diet, characterized by low phosphate and high carbohydrate consumption, may lead to reduced serum phosphate levels in patients at risk for the development of metabolic syndrome.[10] Reduced phosphate levels in the metabolic-syndrome group may represent the consequence of increased transfer of phosphate from the extracellular to the intracellular compartment. Increased insulin levels in patients with metabolic syndrome could be a major determinant of this process.[11]. The activation of sympathetic nervous system observed in patients with metabolic syndrome and the resulting increment in serum catecholamine levels also contribute to the intracellular shift of phosphate.[12] Both insulin and catecholamine stimulate glycolysis, thus increasing the intracellular formation of phosphorylated carbohydrate compounds in the liver and skeletal muscles. The source of this phosphate is the inorganic phosphate of the extracellular fluid; serum phosphate concentrations may decrease rapidly.[13] Lower magnesium concentrations in patients with metabolic syndrome can be attributed to the same mechanisms as lower serum phosphate levels. The patients with high insulin levels showed significantly greater fractional excretion of magnesium is consistent with the hyperinsulinemia-induced renal magnesium wasting. Because both phosphate and magnesium are vital to carbohydrate metabolism, it is possible that the reduced levels of these ions in patients with metabolic syndrome may decrease the peripheral utilization of glucose, thus leading to the development or exacerbation of insulin resistance. In this case, the resulting compensatory

hyperinsulinemia can further decrease phosphate and magnesium concentrations; there is a vicious circle that may contribute to the pathogenesis of metabolic syndrome.[14]The mechanism that causes hypophosphatemia in obesity, revealed by relationship between serum phosphate and BMI, can be attributed to an overconsumption of energy, eg a diet with a low nutrient density, or the result of phosphate depletion due to low protein intake. It is therefore important that both the total energy intake and the relative contributions of carbohydrates, protein and fat should be determined. In obese individuals, an inability to metabolize glucose (possibly due to phosphate depletion), in addition to an increase in serum TG, could be the result of a dietary imbalance of protein, fat and carbohydrates. The relation between serum phosphate and glucose at baseline and between changes in phosphate and glucose over 1 year in men but not in women is another expression of gender difference. Moreover, in men (but not in women) the decrease in glucose associates with a decrease in serum TG. The greater improvement in risk factors for CVD in men than women would appear to be due to higher baseline values. Higher S-TG and serum glucose levels in men than in women have also been reported by Wing RR, et al.[15] Hyperglycaemia could be the result of a reduced capacity to metabolize glucose and experimentally induced chronic hypophosphataemia restricts glucose uptake. Metabolism and the level of serum phosphate affect insulin secretion. In healthy humans, phosphate deprivation stimulates insulin secretion following intravenous administration of a glucose bolus. Elevated TG and reduced HDL-C levels have been referred to as atherogenic dyslipidemia and is thought to be a significant predictor of future high BP and diabetes. Hence the entire metabolic process involving development of hyperglycemia, insulin resistence, hypophosphatemia and atherogenic hyperlipidemia in inter related.[15]

The clinical significance of phosphate disturbances in patients of metabolic syndromes cannot be over emphasized but should be considered as a potential stimulus for targeted interventions whether preventive or therapeutic.

CONCLUSION

The study results further support the need of future research evaluating temporal association between hypophosphatemia and the incidence and complications associated with metabolic syndrome.

ETHICS APPROVAL: The ERC gave ethical review approval.

CONSENT TO PARTICIPATE: written and verbal consent was taken from subjects and next of kin.

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AUTHORS' CONTRIBUTIONS:

All persons who meet authorship criteria are listed as authors, and all authors certify that they have participated in the work to take public responsibility of this manuscript. All authors read and approved the final manuscript.

CONFLICT OF INTEREST: No competing interest declared

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