Metabolic Disturbances of Phosphate in Metabolic Syndrome

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Abstract:

Background: Metabolic syndrome MS a cluster of disorders comprising obesity (central and abdominal), dyslipidaemias, glucose intolerance, insulin resistance (or hyperinsulinaemia) and hypertension – is highly predictive of type 2 diabetes mellitus and cardiovascular disease. It should be emphasized that the metabolic syndrome is a syndrome and not a disease.

The aim of this study is to evaluate the levels of serum phosphate in different levels in subjects with metabolic syndrome MS and Correlation between serum phosphate levels with metabolic syndrome components. The study was carried out at the National diabetes Center (NDC) /AL-Mustansiryia University ,the period from (Desmber.2011 – May 2012) One hundred forty (140) Iraqi individuals enrolled in the study (100 subject diagnosed as having metabolic syndrome and 40 as control group).

The diagnosis of metabolic syndrome was based on Adult Treatment Panel III guidelines. The results of the serum phosphate concentrations in both groups showed that subjects with metabolic syndrome had significantly lower phosphate concentrations 1.52 mg/dl compared with that of control 2.29 mg/dl $P<0.0001$.

The clinical significance of these electrolyte disturbances, as one of the diagnostic criteria of metabolic syndrome. In addition this electrolyte imbalance may have a role in prevention and or treatment of the metabolic syndrome.

Key words: Metabolic syndrome, Serum phosphate, type 2 diabetes mellitus.

Introduction

The metabolic syndrome is described by the clustering of several risk factors for Type 2 diabetes and cardiovascular disease. Lipid disorder, obesity, diabetes in general and high blood pressure are collectively defined as risk factors for cardiovascular disease triggered by metabolic syndrome. The metabolic syndromes have a correlation with the variations in genetic susceptibility, nutritional regiment, physical exercise, chronological age and gender which play direct role in the incidence of metabolic syndrome and its side effects. Clinicians should significantly consider screening all people regardless of age for abnormalities in glucose level. Early treatment in people with abnormal glucose level constitutes a strategy for preventing type 2 diabetes mellitus and metabolic syndrome{1}.

The normal value of Phosphate is 2.5-4.5 mg/dl{2,3} which is a key component of several physiologic pathways, such as skeletal development, bone mineralization, membrane composition, nucleotide structure, maintenance of plasma pH, and cellular signaling.

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Methods and Materials:

One hundred forty (140) Iraqi individuals (100) subject diagnosed as having metabolic syndrome and 40 as control group. their mean age was (20-50) years, all subject were matched by age and sex.

The diagnosis of metabolic syndrome was made according to Adult Treatment Panel III guidelines Metabolic syndrome was defined by the presence of three out of the following features:

An increased waist circumference (> 102 cm for men , > 88 cm for women) Hyperglycemia (fasting glucose≥ 7.0 mmol/L), hypertension systolic/ diastolic pressure ≥ 135/85 mmHg) , dys-lipidemia fasting hypertriglycerides(≥ 1.7 mmol/L) , low HDL- cholesterol(< 1.0 mmol/L in men , < 1.3 mmol/L in women).

Excluded criteria: Full medical history and examination including weigh (wt) while subjects had light clothes and no shoes., high (h), waist circumference (WC) (which was measured midway between the last rib and iliac crest), BMI(body mass index) was calculated as weight in kilograms (kg) divided squared meter (m^2).

Blood pressure was measured by sphygrananometer on the day (examination Hypertension was diagnosed when systolic blood pressure ≥140 mmHg or diastolic pressure ≥90mmHg according to criteria (JNC7) (Joint National Committee 7) based on the overage of 2 readings.

Biochemical Analysis: Blood samples were obtained by overnight fasting after (12-14) h Collect 10 ml blood by venipuncture without turnica From each individual, using 10 ml disposable syringes between 9.00 and 11.00 a.m. The blood sample was divided into two aliquots, the first aliquot blood was put in a plain tube used before clotting for estimation of plasma glucose concentration, the second aliquot was dispensed in a plain tube with gel , allow to clot, and separate serum by centrifugation at room temperature, (3000 rpm) for (10 min). The separated serum was divided into aliquots (100µl) in Ependroff tubes and stored in the freezer about (– 20) C^0 until used for assays. Biochemical analysis of phosphate and glucose by photometric method, concentration were measured by colorimetric method.

Insulin level was determination by (ELISA) to support the presence of hyperlnsulemia and insulin resistance was calculated by HOMA (Homeostatic Model Assessment).

- HOMA=(fasting insulin level (µIU/mL) × fasting glucose level (mmol/L))/22.5
- HOMA=(fasting insulin level (µIU/mL) × fasting glucose level (mg/dl))/405 {4}

Statistical Analysis: Data are expressed as mean ±SD. Unpaired t-test was used for comparisons between study groups, whereas differences in proportions were assessed by using chi-square test. Correlations between phosphate concentrations and metabolic parameters were estimated by using linear regression analysis, whereas multiple regression analysis was used for the multivariate assessment of correlation between phosphate concentration and those variables. *P*-Value of <0.05 defined as statistical significant.

Results

The study involved 100 patients with metabolic syndrome and 40 subjects as control group. There were differences in sex but there were no differences in age, distribution, between study groups. However,

patients with metabolic syndrome had significantly greater body mass index (BMI) and waist circumference values compared with controls. ($P < 0.05$). Patient clinical characteristics were listed in (Table-1). Regarding the Biochemical characteristics of the study participants as expected, patients with metabolic syndrome had significantly greater fasting glucose and insulin concentrations when compared with control.

The results of the serum phosphate concentrations in both study groups show that patients with metabolic syndrome had significantly lower phosphate concentrations ($P< 0.0001$) compared with controls. 90.8% of a patients (89 patients) had abnormally low phosphate concentrations (<2.5 mg/dl) compared with 61.5% of individuals (24 control) in the control group ($P<0.0001$).

Table (1): The age and sex distribution of study groups.

		MS		Control		
		No	%	No	%	
Sex	Male	68	68.0	15	37.5	0.001*
	Female	32	32.0	25	62.5	
Age (years)	<30	7	7.0	5	12.5	0.644
	30---34	11	11.0	4	10.0	
	35---39	12	12.0	7	17.5	
	40-44	19	19.0	8	20.0	
	45---49	31	31.0	12	30.0	
	=>50	20	20.0	4	10.0	
Mean±SD (Range)		42.50±7.34 (24-50)	40.25±8.07 (24-50)			
*Significant p <0.05 level						

Table2: Shows BMI of MS and Control Subject.

BMI (Kg/m2)	MS		Control		
	No	%	No	%	P value
18.5---24.9 Normal weight	2	2.0	14	35.0	0.0001*
25---29.9 over weight	41	41.0	13	32.5	
30---34.9 obese	34	34.0	6	15.0	
=>35 obese class1	23	23.0	7	17.5	
Mean±SD (Range)	107.71±10.42 (85.0-138.0)		92.93±12.22 (74.0-120.0)		
*Significant p <0.05 level					

Table 3:Llevel of S-P, Iinsulin, FPG level and HOMA IR of MS and Control Groups .

	MS		Control		P value
	No	Mean±SD (Range)	No	Mean±SD (Range)	
P (mg/dl)	98	1.52±0.61 (0.76-3.4)	39	2.29±0.43 (1.33-3.1)	0.0001*
Free Insulin (uIU/L)	98	20.83±9.20 (1.7-44.7)	39	3.48±3.05 (1.8-15.23)	0.0001*
FPG (mg/dl)	100	195.33±66.22 (100.0-385.0)	40	100.45±9.59 (72.0-113.0)	0.0001*
HOMA IR Concentration	98	10.72±7.88 (0.86-38.33)	39	0.70±0.40 (0.36-2.61)	0.0001*
*Significant <0.05 level					

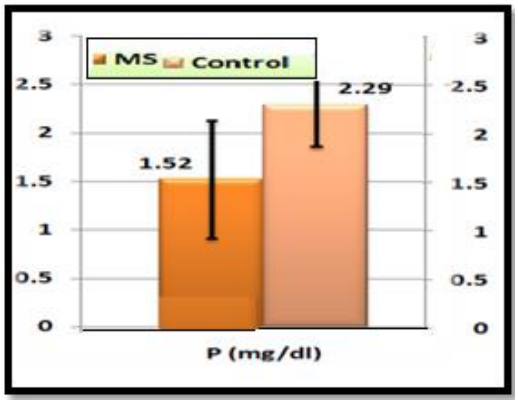

Fig:1 Deference of S-P concentration among patients with MS and control (p = 0.0001)

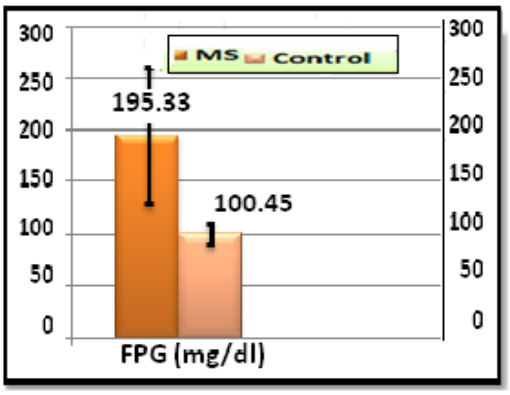

Fig:2 Deference of FPG concentration among patients With MS and control (p = 0.0001)

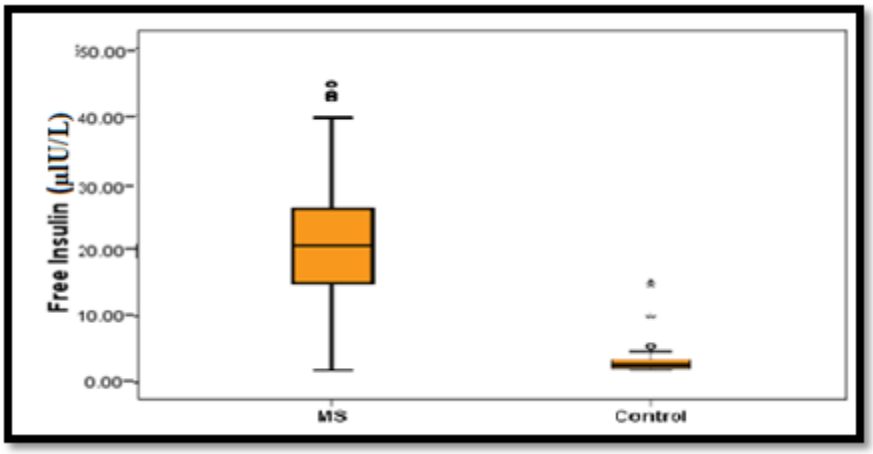

Fig: 3 Free insulin (µIU/L) level of metabolic syndrome and Control subject.

Discussion:

Serum phosphate and glucose :-

Our study show significant difference in FPG levels between patients with MS (195.33±66.22) and control (100.45±9.59) mg/dl (p <0.0001) as. shown in fig (2), also mean levels of S-P showed significantly deference between patients with MS (1.52±0.61) mg/dl when compared with healthy subject (2.29±0.43) mg/dl as shown fig(1) and table (3). Also the results showed that serum phosphate had negative correlation with glucose r=-0.392 P<0.0001..

Our result have been consistent with the findings Wan Park, et. al 2009 {5} and Rigas Kalaitzidis et al, 2005{6} found that patients with metabolic syndrome were low S-P compared with healthy. a reduced level of serum phosphate in patient 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 concentrations, leading to the development of vicious circle that may contribute to the pathogenesis of metabolic syndrome.{6}. Also found negative correlation between S-P and FPG related to phosphate is vital to carbohydrate metabolism{6}. Haap et al show that a low serum phosphate level was associated with reduced insulin sensitivity {7} A high body mass index in subjects with low

phosphate level may result, at least in the part from reduce dietary intake {8}.

Serum phosphate and HOMA-IR:-

The result revealed that the mean of Insulin level showed significant difference between patients with MS 20.83±9.20 and control (3.48±3.05) (p <0.0001) as shown in fig (3).

Also our result showed S-P level had negative significant correlation with IR (r=-0.339).

In 2011Timothy Ellam *et al*.{9} found that mice with low phosphate intake induces insulin resistance. These data indicate for the first time that controlling dietary phosphate intake may influence development of both atherosclerosis and the metabolic syndrome **.**

Low dietary phosphate intake has not previously been demonstrated to induce insulin resistance, adiposity, or steatosis,

Also Celik. *et al* 2011{10}and P Giram in 2010{11} fond that when serum phosphate level was low insulin resistance increase .

The induction of insulin resistance by low dietary phosphate intake may reflect reduced glycolytic phosphometabolite synthesis due to intracellular phosphate depletion. Inhibition of glycolysis under conditions of phosphate depletion has been documented previously{12} and a phosphate infusion increases the glucose disposal rate (insulin sensitivity) in healthy subjects during euglycemic insulin infusion{12}.

Haglin presented a hypothesis in 2001 suggesting that low serum phosphate is the cause of the disturbed metabolism in the metabolic syndrome. This was based on the fact that serum phosphate is an important component of energy metabolism.

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الاضطرابات الأيضية للفوسفاتِ في المتلازمةِ الأيضيةِ

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*** وزراة العلوم والتكنولوجيا.

الخلاصة:

المتلازمة الأيضية - مجموعة من الاضطرابات التي تضم السمنة (البطن الوسطى)، زيادة نسبة الدهون ارتفاع السكر في الدم ، مقاومة الأنسولين وارتفاع ضغط الدم –التبوء بمرض السكري من النوع الثاني وأمراض القلب والأوعية الدموية.

وينبغي التأكيد على أن متلازمة التمثيل الغذائي هي متلازمة وليس مرضا. كان الهدف من الدراسة لتقيم ثاثير المستويات المختلفة للفسفور في مرضى المتلازمة الايضية و تحديد علاقة الفسفور مع مكونات المتلازمة الايضية.

اجريت الدراسة في المركز الوطني للسكر في الجامعة المستنصرية، ضمت الدراسة 140 فرد عراقي من كلا الجنسين (100 تم تشخيصهم بأنهم مصابون بالمتلازمة الايضية، و 40 أصحاء) تتراوح أعمارهم 20-50 سنة ونم استبعاد المرضى الذين يتعاطون علاج مرض السكري او ضغط الدم.

تشير النتائج الى انخفاض مستوى الفسفور لدى االعراقيون المصابون بمتلازمة الايض (التمثيل الغذائي) 1.52 mg/dl مقارنة مع الأصحاء 2.29 mg/dl وبنسبة 98% و 61.5% على التوالي P<0.0001 ان هذا الاضطراب يمكن اعتباره واحد من وسائل المساعدة في تشخيص المتلازمة الايضية.

الأهمية السريرية لهذه الاضطرابات ، باعتبارها واحدة من المعايير التشخيصية لمرضى متلازمة التمثيل الغذائي. وبالإضافة إلى ذلك قد يكون لها دور في الوقاية والعلاج من متلازمة التمثيل الغذائي