Original Article

RELATIONSHIP BETWEEN S-INSULIN AND CHROMIUM, MANGANESE, COBALT, AND ZINC EXCRETION IN THE URINE IN HEALTHY KHYBER PAKHTUNKHWA PERSONS

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ABSTRACT

Objective: *Clinical research has shown that mineral imbalances, including those involving zinc, cobalt, manganese, and chromium, are crucial for the onset and development of diabetes mellitus. To ascertain the function of these trace elements in pathogenesis and the advancement of type 2 diabetes, this investigation aimed to ascertain if there was a link, if any, between the urine excretion of these minerals and s-insulin levels.*

Study Design: *Cross-sectional study.*

Place and Duration of study: From January to December 2013, this research was carried out at Khyber Medical University (KMU), Peshawar, at the Institute of Basic Medical Sciences (IBMS).

Materials and Methods: *This research comprised 200 healthy people from the seven divisions of Khyber Pakhtunkhwa (Abbottabad, Peshawar, Mardan, Bannu, Dera Ismail Khan, Malakand, and Kohat) with normal fasting blood sugar (FBS), creatinine, cholesterol, HDL, LDL, and TAG values. Anthropometric measures and demographic data were recorded. Serum creatinine, serum insulin, lipid profile, and fasting blood sugar were measured using a blood sample. Urine samples were taken early in the morning to measure zinc, cobalt, manganese, and chromium levels.*

Results: *It was discovered that there was a near-to-significant negative connection (r: -0.127, p: 0.073) between manganese and s-insulin and a considerably high negative correlation (r: -0.191, p: 0.007) between chromium and s-insulin. Thus, elevated chromium and manganese excretion in the urine in healthy persons may eventually cause T2DM to proceed if improperly managed.*

Conclusion: *the present study revealed a significant correlation of s-insulin with urinary excretion of chromium only.*

Keywords: *Type II diabetes mellitus, s-insulin, trace elements.*

INTRODUCTION

Diabetes mellitus, a metabolic syndrome, is caused by a deficiency in insulin production (type I) or by resistance to the insulin produced (type II). It is characterized by chronic hyperglycemia with disturbances in carbohydrate, fat and protein metabolism arising from a defect in insulin secretion, its action, or both [1].

As of right now, diabetes mellitus lacks a succinct description. The National Diabetes Data Group released the most widely accepted definition of diabetes. The word "diabetes mellitus," which encompasses four distinct forms of the condition, is described as "a chronic hyperglycemic state which may result from numerous genetic and environmental factors" and induces instability in the metabolism of proteins, lipids, and carbs [2].

Clinical study indicates that diabetes mellitus might cause disturbances in the trace element homeostasis. Conversely, studies also indicate that early abnormalities of some trace elements may disrupt

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normal glucose and insulin metabolism. Chronic hyperglycemia may lead to significant alterations in the metabolism of several microelements, but some of these nutrients may also directly affect glucose homeostasis [3, 4]. Regarding the important trace elements, most research focuses on the status of specific elements, either alone or in various combinations, and the consequences of deficiency on the organism. In some chronic conditions, the gastrointestinal tract (GIT) may not absorb certain trace elements properly, leading to deficiencies in certain minerals [4, 5]. different investigations have shown that an individual's shortage in certain elements, such as Cr, Mn, Zn, Mg, and Co, may cause glucose intolerance and accelerate the development of different issues related to diabetes mellitus [6]. Trace elements may have particular roles in the pathophysiology and development of type II diabetes mellitus, according to theories. This study mainly focused on exploring the aspect of the likely progression towards type-II Diabetes mellitus vis-a-vis the excretion of four trace elements, Chromium, Manganese, Cobalt and Zinc, in the urine of hitherto healthy individuals.

MATERIALS AND METHODS

In the research, a cross-sectional design was used. From January to December 2013, the Institute of Basic Medical Sciences (IBMS) in Peshawar was the site of this investigation. Through non-probability sequential sampling, two hundred healthy men and women between the ages of 18 and 50 from each of Khyber Pakhtunkhwa's seven divisions—Abbottabad, Peshawar, Mardan, Bannu, Dera Ismail Khan, Malakand, and Kohat—were included in the research. Patients with a history of type 2 diabetes and those with FBS levels more than 126 mg/dl were not allowed to participate in the trial. This research excluded all pregnant women, patients with cancers of any kind, including leukaemia, lymphomas, carcinomas of the breast, colon, and prostate, and those with chronic illnesses such as hypertension, lipid disorders, coronary heart disease, and endocrine disorders.

DATA COLLECTION

Before the research began, clearance from the ethical committee was secured. Individuals gave their permission after being informed of the study's risks and benefits. The research included the normotensive individuals who met the inclusion criteria with normal FBS, creatinine, cholesterol, HDL, LDL, and triglycerides. The respondents' anthropometric data, including height, weight, waist/hip ratio, and their name, age, and gender, were noted. In the central laboratory of the Institute of Basic Medical Sciences (IBMS), Khyber Medical University, Peshawar, six to eight millilitres of blood were drawn from fasting individuals to determine their fasting blood sugar (Kit: GLUC2 Glucose HK), lipid profile, which included cholesterol (Kit: CHOL2 Cholesterol Gen.2), HDL-cholesterol (Kit: HDLC3 HDL-cholesterol plus 3rd generation), LDL-cholesterol (Kit: LDL_C LDL Cholesterol) and triglycerides (Kit: TRIGL Triglycerides), and serum-creatinine (Kit: CREJ2 Creatinine Jaffe' Gen.2 (compensated)). Roche Diagnostic, Germany, provided the kits. Through the generosity of Peshawar Laboratory, Peshawar, serum insulin was tested using an ELECSYS 2010 Immunoassay analyzer and a kit provided by Roche Diagnostic Germany.

Atomic absorption spectrophotometry was used at the National Center of Excellence in Analytical Chemistry (NCEAC), University of Sindh, Jamshoro, Pakistan, to measure the urinary levels of trace elements. Urine samples were taken early in the morning from fasting patients in polyethene bottles (Italy, Kartell1, Milan) and sterilized with acid to determine urinary chromium, manganese, cobalt, and zinc. A home microwave oven with a maximum heating capacity of 900 W was used to digest the samples. Urine samples were tested for trace elements using a Perkin-Elmer model A Analyst 700 (Norwalk, CT, USA) atomic absorption spectrometer, GF 3000 with background correction, and a graphite furnace HGA-400. Mg(-NO3)2, a chemical modifier, was used with radiation sources and hollow cathode lamps to determine the amount of chromium.

DATA ANALYSIS

The data were input and examined using SPSS 17.0. The information was tallied and reported as mean + SEM.

RESULTS

The participants' average age was 33.39±9.62 years. There were 200 people total, including 104 men and 96 women. Tables 1, 2, and 3 present the findings of anthropometric measurements (height, weight, BMI, diastolic and systolic blood pressure), laboratory parameters (FBS, s-creatinine, s-insulin, cholesterol,

Table 1: Anthropometric measurements of study population

	Age	Height	Weight	BMI	W/H	BP (mm Hg)	
	(Year)	(cm)	(Kg)	(Kg/m^2)	Ratio	Systolic	Diastolic
Mean	33.39	166.9	66.82	24.13	0.93	117.89	77.95
SD	9.62	9.43	11.37	3.66	0.15	10.54	5.33

Table 2: Blood/serum levels of biochemical parameters

	FBS	Creatinine	s-Insulin	Cholesterol	HDL	LDL	TAG
	(mg/dl)	(mg/dl)	(µU/ml)	(mg/dl)	(mg/dl)	(mg/dl)	(mg/dl)
Mean	85.46	0.66	15.07	170.19	38.46	111.15	148.22
SD	10.73	0.34	20.32	48.45	12.21	71.50	91.19

Table 3: Urinary excretion of trace elements in study population

	Chromium	Manganese	Cobalt	Zinc	HDL	LDL	TAG
	(mg/dl)	(mg/dl)	(µU/ml)	(mg/dl)	(mg/dl)	(mg/dl)	(mg/dl)
Mean	85.46	0.66	15.07	170.19	38.46	111.15	148.22
SD	10.73	0.34	20.32	48.45	12.21	71.50	91.19

Table 4: Correlation between s-insulin and urinary Cr, Mn, Co and Zn

	Chromium	Manganese	Cobalt	Zinc
	(µg/L)	(µg/L)	(µg/L)	(mg/L)
Pearson Correlation (r)	-0.191**	-0.127	-0.075	-0.078
p. Values	0.007	0.073	0.290	0.273

**r is highly significant at the p: 0.01 level (2-tailed)

Table 5: Distribution of correlation between s-insulin and urinary excretion of chromium, manganese, cobalt and zinc in different divisions of KPK

Division		Chromium	Manganese	Cobalt	Zinc
		(µg/L)	(µg/L)	(µg/L)	(mg/L)
Abbottabad	Pearson Correlation (r)	0.474*	0.310	0.173	0.260
	p. Values	0.017	0.132	0.410	0.209
	Number	25	25	25	25
Peshawar	Pearson Correlation (r)	-0.358*	-0.270	-0.114	-0.091
	p. Values	0.011	0.058	0.430	0.531
	Number	50	50	50	50
Mardan	Pearson Correlation (r)	-0.043	-0.080	0.006	0.044
	p. Values	0.840	0.705	0.978	0.835
	Number	25	25	25	25
Kohat	Pearson Correlation (r)	0.101	-0.065	-0.142	-0.196
	p. Values	0.632	0.756	0.500	0.348
	Number	25	25	25	25
Bannu	Pearson Correlation (r)	-0.210	0.002	0.152	0.077
	p. Values	0.314	0.992	0.470	0.715
	Number	25	25	25	25
D.I.Khan	Pearson Correlation (r)	0.027	-0.123	-0.163	-0.378
	p. Values	0.899	0.559	0.435	0.063
	Number	25	25	25	25
Malakand	Pearson Correlation (r)	-0.322	-0.459*	0.071	0.227
	p. Values	0.116	0.021	0.735	0.275
	Number	25	25	25	25

* r is significant at the p: 0.05 level (2-tailed). ** r is highly significant at the p: 0.01 level (2-tailed).

HDL, LDL, and triglyceride), and trace element levels in the urine of all 200 subjects, expressed as mean + SD.

DISCUSSION

Research was undertaken on a healthy adult population in Lahore to identify the reference range of zinc in serum. The results showed that the mean + SEM value of zinc in serum was 24.02 + 7.03 µmol/L [7]. Another recent research on the Nigerian population revealed that those with diabetes mellitus had considerably lower mean blood concentrations of zinc, magnesium, selenium, and cr than their healthy, non-diabetic counterparts [8]. In a similar vein, Indian population research comparing people with diabetes to those without the disease revealed that diabetic patients had very low blood levels of zinc and magnesium, which were caused by higher losses in their urine [9].

The excretion of Cr in the total (200 subjects) was lower than that recorded by Kazi et al. [13] and Esfahani et al. [14] but higher than that of Swedish subjects described by Rodushkin [12]. In contrast, it was lower than that of the Italian and Canadian populations reported by Minoia et al. [10] and Vankatesh and Jost [11]. The amount of Mn excreted by the Swedish individuals 12 was similar to that of the Italian, Canadian 11, Hyderabad (Pakistan), 13, and Iranian persons 14, although it was of lesser quantity. The excretion of cobalt (Co) was somewhat similar with Canadian people 11 but not with populations of Italians 10, Swedish 12, Hyderabad (Pakistani) [13], and Iranians 14. Zinc excretion via the urine was not similar to any group that has been documented [10, 11, 12, 13, 14, 15].

Except for the male Kohat subjects, whose excretion of Cr was greater than that of the Italian [10] subjects, all seven divisions of Khyber Pakhtunkhwa showed close agreement with the Italian 10 and Canadian 11 individuals. Its excretion, however, was reduced in Hyderabad (Pakistan) 13 and Iranian 14 patients and greater in Swedish 12. The Mn excretion was comparable to the population of Sweden 12. The population of Hyderabad (Pakistan), Italians 10, Canadians, and Iranians [11, 12, 13], was different. Italian and Swedish reports indicated that the excretion of Co in the urine of healthy persons was high at 10 and 12 but somewhat greater for Canadians 11. On the other hand, although the highest amounts of Co varied from one another, the lowest values were similar. In all seven divisions of Khyber Pakhtunkhwa, the population's urinary excretion of zinc was greater than that of Italian, Swedish, Canadian, Pakistani, and Iranian (Hyderabad residents).[11, 12, 13, 14, 15].

In the Khyber Pakhtunkhwa study population, a significantly significant negative association (r:-0.191, p: 0.007) was seen between urine chromium and s-insulin. Table 4 shows a near-to-significant negative connection (r: -0.127, p: 0.073) between manganese and s-insulin. Co and Zn did not, however, significantly correlate with s-insulin.

Current research has shown that blood chromium increases cellular sensitivity to insulin [15], and manganese is involved in the production and release of s-insulin [16]. As a result, cellular deficiencies in both of these components may result in insulin resistance or insulin imbalance, which may cause the patients to advance toward type II diabetes mellitus. Since there was no discernible relationship between urinary zinc and cobalt levels and s-insulin, likely, the excretion of these two elements in the urine of non-diabetic people did not affect s-insulin levels. Nonetheless, further validation of the results of this investigation would be very beneficial from a reexamination of the same participants.

CONCLUSION

The current investigation finds a near-to-significant negative association between s-insulin and urine Mn excretion and a substantial negative correlation between s-insulin and urinary Cr excretion. Therefore, it follows that increased excretion of these two components would cause an imbalance in the blood's insulin amount. This is because the proper levels of Mn in the blood are necessary for the synthesis and secretion of insulin. If urinary excretion of Mn rises, the amount of Mn in the blood will decrease, jeopardising insulin synthesis and secretion.

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