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Original Article

Biochemical assessment of uric acid and magnesium in prediabetic patients in Peshawar-KP: A case-control study.

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Abstract

Background: Background: There is a lack of information regarding serum uric acid (SUA) and magnesium levels among the pre-diabetics population. This study aimed to assess the biochemical assessment of both uric acid and magnesium in prediabetics of the Peshawar-KP region.

Methodology: In this case-control study, patients having normal glucose levels were considered as control, and prediabetics were cases. Fasting blood glucose (FPG) levels between 100-125 mg/dl or HbA1c levels between 5.7 to 6.4% were considered pre-diabetic. SUA was assessed by the Uricase method, serum Mg+ by the Calmagite calorimetric method, and fasting glucose was assessed by the GOD-POD enzymatic method.

Results: According to our findings, mean values of serum magnesium were 2.12 ± 0.60 mg/dl (p=0.026) and 1.10 ± 0.82 mg/dl (p=0.001) in male and female of control group whereas, 1.60 ± 0.44 mg/dl (p=0.004) and 0.90 ± 0.22 mg/dl (p=0.002) in male and female of cases group respectively. Correspondingly, mean value of SUA was recorded as 4.14 ± 0.66 mg/dl (p=0.008) and 3.12 ± 0.38 mg/dl (p=0.004) in male and female of control group whereas 8.10 ± 1.00 mg/dl (p=0.002) and 6.22 ± 0.44 mg/dl (p=0.003) in male and female of cases and subjects group respectively. It is noticeable that mean serum magnesium and SUA values were higher in the male of both groups compared to females.

Conclusion: The study concluded that lower serum magnesium levels in prediabetics might result from the closure of K+ channels, defective phosphorylation of insulin receptors, or diminished glucokinase activity. Higher uric acid levels in prediabetics might result from inflammation, oxidative stress, and hypertrophy of the tubules.

Keywords

Pre-diabetics, Hypomagnesemia, Hyperuricemia, Diabetes Mellitus.

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Introduction

The term pre-diabetes refers to serious health conditions where the blood sugar levels are elevated than the normal ones but not so much elevated to be diagnosed as diabetes type 2. More or less, 84% of prediabetics are ignorant about their condition. Prediabetics are at a higher risk of developing type 2 diabetes with stroke and heart diseases[1]. Lifestyle modification is necessary to avoid the disease because 15 to 30% of patients might develop diabetes mellitus (DM) within five years[2].

Better management of the body's cholesterol, blood pressure, and blood glucose levels and quitting smoking could decrease diabetes-related symptoms and its acute and chronic manifestation[3]. A report by Center for Disease Control and Prevention (CDC), depression is a major risk factor in developing diabetes in the US[4]. Despite the CDC report, several other reports also mentioned depression as a major risk for pre-diabetes and diabetes[5-9]. In this scenario, earlier identification of pre-diabetes and diabetes in people with a depressive state is significantly important to preserve their lives.

In glucose metabolism, the role of magnesium is considered to be very important, and this is because magnesium acts as a co-factor for numerous enzymes in insulin secretion, insulin homeostasis as well as insulin binding. A reduced level of magnesium results in increased resistance to insulin[10]. There are two mechanisms through which uric acid is synthesized in the body, one through purine breakdown and the second through direct synthesis from 5-phosphoribosyl pyrophosphate and glutamine. Age and sex are two factors that directly affect the serum urate.

Uric acid is a powerful antioxidant agent that results in insulin resistance, an increase in oxidative stress, dysfunction of endothelium, and an activated renin-angiotensin (RA) system, which is linked with cardiovascular risk factors, hypertension, and abnormal metabolism of glucose and metabolic syndrome[11,12]. An earlier assessment of SUA and serum magnesium in prediabetics will be a helping tool in reducing the development of DM and associated complications.

Several/epidemiologic studies have reported that high serum levels of uric acid are strongly associated with prevalent health conditions such as obesity, insulin resistance, metabolic syndrome, diabetes, essential hypertension, and renal disease[4]. Population-based studies have shown that hyper-uremia is an independent risk factor for cardiovascular disease (CVD). This association is particularly robust among individuals at high risk for CVD, including those with obesity, hypertension, diabetes, and renal disease. With the above background, this study examined the serum level of uric acid in diabetics, pre-diabetics, and controls[13].

There is a lack of information regarding SUA and magnesium levels among the pre-diabetics population. So the rationale of the study is to explore the same and add valuable information to the literature.

Methodology

This case-control study was conducted in a private teaching hospital in Peshawar from January to September 2021. The IRB of the concerned hospital approved the study (Letter No: NTH/09/2020). Out of 421 screened individuals, 300 were enrolled in the study. The sample size was calculated using the WHO calculator, which was 292.

Inclusion Criteria

Subjects having FPG 100-125 mg/dl or HbA1c levels between 5.7 to 6.4% were included in the study and were labeled as cases, while those having FPG 70-100 mg/dl or HbA1c value less than 5.7% or absence of criteria that matches pre-diabetes were labeled as controls.

Exclusion Criteria

All subjects with known type I or type II DM, cardiovascular diseases, GI tract diseases, renal and pulmonary diseases, Gout, cancer, pregnant and lactating women, Mg+ supplementation, and hypertension were excluded. Furthermore, individuals with self-reported hepatic, kidney, and

cardiovascular disorders were also excluded from the study.

Groups

Individuals with normal glucose levels were considered as control, and those with impaired glucose levels as prediabetics and were labeled as cases. Each group contained 150 individuals, including males and females. Informed consent was taken from all the individuals at the beginning of the study.

General data acquisition

Data of all the anthropometric characteristics were recorded using a brief questionnaire form. Body mass index (BMI) was recorded by taking weight in kilograms and height in cm.

Laboratory procedures and blood collection

After observing an overnight fasting period, 5ml intravenous blood was taken from the individuals. All the blood samples were transferred into a chilled chamber and carried to the hospital's biochemistry lab for further procedure. The serum of all the collected blood samples was separated using a centrifuge machine (Beckman centrifuge) at a speed of 3200 rpm for 12 min.

After separating the serum, a biochemical analysis of the pre-determined parameters was done. The analysis was carried out using an automated analyzer (Bioevopeak BA-A-120). Serum uric acid of both the groups, serum Mg+ and fasting plasma glucose, were assessed using standard methods and guidelines (Uricase, Calmagite calorimetric, and GOD-POD enzymatic method), respectively.

Statistical analysis

Results were analyzed using statistical software SPSS version 20.0. A p-value less than 0.05 was considered significant, and a sample T-test was done to compare both groups.

Results

Out of 421 screened individuals, 300 were enrolled in the study; among them, 208 were male, while 92 were female. The mean age for all the study population was 36.4 ± 12.4. The study revealed the percent prevalence of pre-diabetes in men was 46.66% (n=104) and 53.33% (n=46) in women, respectively. The demographic characteristics of the two groups regarding gender, age, BMI, education, residential area, smoking habits, etc., are shown in Table 1 below.

Table 1: Demographic characteristics of the study individuals.

Variables		Total (n=300)	Control (n=150)	Cases (n=150)
Gender	Male	208(69.33)	104(69.33)	104(69.33)
	Female	92(30.67)	46(30.67)	46(30.67)
Age (years)		36.4±12.4	34.2±10.0	37.0±14.6
Education	Primary/Middle	169(56.33)	91(60.67)	78(52.00)
	Graduate	98(32.67)	40(26.67)	58(38.67)
	Postgraduate	33(11.00)	19(12.67)	14(9.33)
Area	Urban	100(33.33)	52(34.67)	48(32.00)
	Rural	200(66.67)	98(65.33)	102(68.00)
Smoking Status	Non-smoker	118(39.33)	62(41.33)	56(37.33)
	Ex-smoker	142(47.33)	66(44.00)	76(50.67)
	Current smoker	40(13.33)	22(14.67)	18(12.00)

According to our findings, mean values of serum magnesium were 2.12 ± 0.60 mg/dl and 1.10 ± 0.82 mg/dl (p=0.034) in male and female of control group whereas, 1.60 ± 0.44 mg/dl and 0.90 ± 0.22 mg/dl (p=0.001) in male and female of cases group respectively. Correspondingly, the mean value of serum uric acid was recorded as 4.14 ± 0.66 mg/dl and 3.12 ± 0.38 mg/dl (p=0.020) in the male and female control groups, whereas 8.10±1.00

mg/dl and 6.22 ± 0.44 mg/dl (p=0.022) in male and female of cases and subjects group respectively. It is noticeable that mean serum magnesium and SUA values were higher in the male of both groups compared to females. The results demonstrated mean lower levels of serum magnesium and higher levels of serum uric acid in prediabetics of the Peshawar-KP region (Table 2).

Table 2: Serum Mg+ and SUA in control and cases groups.

Variables	Control			Case		
	Male	Female	p-value	Male	Female	p-value
Serum Mg+ (mg/dl)	2.12±0.60	1.10±0.82	0.034	1.60±0.44	0.90±0.22	0.001*
Serum UA (mg/dl)	4.14±0.66	3.12±0.38	0.020	8.10±1.00	6.22±0.44	0.022*

*p<0.05 is considered significant.

Discussion

To the best of our knowledge, this is the first study on Peshawar residents to assess serum Mg+ and serum uric acid levels in individuals with pre-diabetes. The study revealed the percent prevalence of pre-diabetes in men was 46.66% and 53.33% in women, respectively. The higher incidence of pre-diabetes in women than in men might be due to the deposition of excessive abdominal fats. The fat accumulation can result in impaired glucose tolerance and insulin resistance because of innate immunity activation due to white adipose tissue inflammation. This mechanism also results in the down-regulation of adiponectin, which acts as an insulin-sensitizing effector.

Additionally, insulin resistance can be the result of hypo-adiponectinemia[8]. According to our findings, the mean value of serum uric acid was recorded as 4.14 ± 0.66 mg/dl and 3.12 ± 0.38 mg/dl (p=0.020) in the male and female control group, whereas 8.10 ± 1.00 mg/dl and 6.22 ± 0.44 mg/dl (p=0.022) in male and female of cases and subjects group respectively. The values were found to be higher in males in comparison to females in both study groups. A cross-sectional study conducted in Thailand demonstrated an association of an increased SUA with that fasting plasma glucose level[14]. This study was restricted to elderly patients, and no gender stratification was considered while conducting this study. Another cohort study having US origin revealed that induced levels of SUA present a risk factor individually for pre-diabetes[15]. Another cohort study in the Netherlands revealed a positive connotation of SUA with pre-diabetes in subjects with normal glycemic levels[16,17]. The study suggested the role of SUA in developing DM in early phases compared to the late phase mechanism. This study further revealed a strong association between SUA and pre-diabetes in women compared to men.

The connotation between SUA and glucose metabolism got many biological clarifications. Some of the clarification is that, firstly, cells induce inflammation and oxidative stress when they get exposed to uric acid[18]. This inflammation and oxidative stress results in developing insulin resistance, which is the central mechanism in the onset of DM. Moreover, the higher SUA levels may be a reason for a remarkable decrease in adenosine monophosphate-activated protein kinase activity, resulting in increased glucose production by the liver[19]. The role of Mg+ in managing various metabolic syndrome, cardiovascular illness, cerebrovascular coincidence, HTN, and type DM2 has established excessive attention in recent decades[20,21]. Lower levels of Mg+ contribute to complications, insulin resistance, and higher blood glucse[22].

The results of this study further revealed the mean values of serum magnesium as 2.12 ± 0.60 mg/dl and 1.10 ± 0.82 mg/dl (p=0.034) in the male and female control groups, whereas 1.60 ± 0.44 mg/dl and 0.90 ± 0.22 mg/dl (p=0.001) in male and female of cases group respectively. The mean values were higher in males compared to females in both groups. The reason might be the results of closure of K+ channels, defected phosphorylation of insulin receptors, or diminished activity of glucokinase. Intervallic determination of Mg+ levels in the body must be done to avoid

complications associated with its deficiency, and appropriate Mg+ replacement should be considered.

Higher renal secretion of magnesium abridged tubular reabsorption because of insulin resistance, and insulin insensitivity (which affects intracellular magnesium transport) are generally the results of osmotic diuresis, which causes low quantities of magnesium in prediabetics. Moreover, these reduced magnesium levels result in postprandial impaired action of insulin, the defective activity of tyrosine kinase, and the worsening of insulin resistance in prediabetics. Though numerous studies have scrutinized the association between magnesium and diabetes, there are few studies on the association of magnesium with pre-diabetes and its development of DM.

The findings of our study are consistent with the result shown in some other studies[23-25]. Another study revealed positive effects of Mg+ supplementation in glucose metabolism disorders and management[26]. Our study has a few limitations, including limited literature showing the available regional data, a smaller sample size, and a single hospital for data collection. Further studies with larger sample sizes and multicenter data have been suggested to check the reliability of both Mg+ and SUA in prediabetics before the onset of DM.

A comprehensive search was done in order to reduce the possibility of any publication bias. Begg's test was performed, which revealed no publication bias.

Conclusion

The study revealed the percent prevalence of pre-diabetes in men and women, respectively. The SUA values were higher in males compared to females in both the study groups, which indicates that higher levels of SUA can result in the onset of pre-diabetes and, ultimately, DM. Similarly, mean serum Mg+ values were lower in cases compared to the control group (healthy individuals), which confirms that Mg+ deficiency might play a potential role in developing pre-diabetes leading to DM. Additionally, the values were more in males as compared to females. Therefore, a close check on the SUA and Mg+ should be kept to avoid the onset of DM symptoms.

Conflicts of Interest

The authors have declared that no competing interests exist.

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