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Association of serum magnesium and glycated hemoglobin in type 2 diabetes mellitus

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Abstract
Background: Diabetes is a chronic metabolic disease characterized by elevated levels of blood glucose, which leads over time to serious damage to organs. Magnesium (Mg) is the second most plentiful intracellular cation after potassium. It's show a role in glucose transport through cell membrane.
Aims: The study was scheduled to measure the effect of serum magnesium level in type 2 diabetic patients and to compare it with that of healthy subjects and to match the obtained serum magnesium levels with glycemic control of the patients assessed by glycated hemoglobin (HbA1c) value, obesity, and presence of diabetic complication.
Patients and Methods: The study was case control, it carried out at Department of Biochemistry, College of Medicine, University of Baghdad and at Diabetes Center of Marjan Teaching Hospital in Al-Hilla City during the period from July 2020 to October 2020. It included 100 subjects 50 patients with type 2 diabetes mellitus (T2DM) and 50 apparently healthy subjects served as control group.
Results: The results showed that Mean±SD value of serum magnesium of T2DM patients was significantly lower than that of controls group ($p \leq 0.0001$). The mean value of serum magnesium was significantly decreased in obese diabetic patients when compared with overweight and normal weight patients ($p \leq 0.0001$). The mean value of serum magnesium was also significantly lower in diabetic patients who had HbA1c > 8.5% in comparison with those had HbA1c 7- < 8.5% ($p \leq 0.031$) and < 7% ($p \leq 0.0001$).
Conclusion: Type 2 diabetic patients suffered significantly from magnesium deficiency that is significantly associated with poor diabetic control and obesity.

Keywords: Type 2 D.M, Serum Magnesium, Obesity

Introductions

Diabetes mellitus (DM), commonly known as diabetes, it is a chronic, metabolic disease characterized by elevated levels of blood glucose, which leads over time to serious damage to the heart, blood vessels, eyes, kidneys and nerves [1]. Diabetes mellitus is classified into four broad categories: Type 1 diabetes, type 2 diabetes, gestational diabetes, and "other specific type. The "other specific types" are a collection of a few dozen individual causes [2]. The prevalence of diabetes has been increasing exponentially, both in developing and developed nations. In 2019, the prevalence of diabetes among adults (Age 20-79 years) was 436 million worldwide [3]. Diabetes is the leading cause of cardiovascular and kidney disease, and the most common preventable cause of blindness worldwide among working age adults (20-65 years) [4]. The chronic complications of diabetes are broadly divided into micro vascular and macro vascular [5]. Studies show that early tight glycemic control slows the progression and development of diabetic autonomic neuropathy and micro vascular complications [6]. The progression of these complications can lead to loss of visual, renal, and neurologic functions, impaired mobility and cognition, poor quality of life, if left uncontrolled or untreated, they lead to irreversible damage and even death [7]. There is a need to increase awareness that DM is a generalized disorder that encompasses multi organ involvement and accordingly leads to a myriad of complications [8]. Diabetes is also linked to other health problems such as sleep apnea, depression, and dementia [9]. Aim of this study to measure the effect of serum magnesium level in patients with type 2 diabetes mellitus and to compare it with that of healthy subjects and to match the obtained serum magnesium levels with glycemic control of the patients assessed by glycated hemoglobin (HbA1c) value,

obesity, and presence of diabetic complication, ischemic heart disease hypertension and gender.

Methods and Materials

Study Design: A case control study.

Study Setting: The case control study was achieved at Biochemistry Department, College of Medicine, and University of Baghdad and at Diabetes Center of Marjan Teaching Hospital in Al-Hila City, during period from July 2020 to October 2020. It included 100 subjects; 50 patients with type 2 diabetes mellitus (T2DM) and 50 healthy control subjects.

Data Analysis: The Statistical Package for Social Sciences (SPSS version 23) was used to achieve the statistical analysis. Analysis of Variance and Student's t-tests were used to test for statistical significance. Linear regression was utilized to test the correlation between different studied parameters, the significance of the r-value was assessed by related p value. A *p*-value of ≤ 0.05 was considered significant.

Results: The Mean±SD values of age of patients group was (58.80±6.18years) and of controls group was (56.48±6.34years) with no significant difference between them. (Table 1). The results of this study revealed non-significant differences in mean values of blood HbA1c and serum magnesium levels between males and females in each of diabetics group and controls group (Table 2).

Depicts that mean±SD value of serum magnesium levels of obese diabetic patients (1.36±0.19 mg/dl) was significantly lower than that of overweight (1.76±0.38 mg/dl) and normal weight (1.60±0.402 mg/dl) diabetic patients (For both $p \leq 0.0001$), with no significant difference between normal weight and overweight ones (Table 3).

There is significant decrease in mean value of serum magnesium concentrations in diabetic patients who had poor glycemic control, HbA1c > 8.5% (1.42±0.29 mg/dl) and those had fair glycemic control, HbA1c 7- < 8.5% (1.59±0.30 mg/dl) when compared with patients had well glycemic control, HbA1c < 7% (1.92±0.34 mg/dl, $p \leq 0.0001$, $p \leq 0.031$, respectively), without significant difference between well controlled and fair controlled diabetic patients (Table 4). The correlations among the measured demographic and laboratory parameters of healthy controls group. The values of BMI was significantly positively correlated with each of random serum glucose levels (r = 0.363; $p \leq 0.01$ Figure 3.2) and HbA1c values (r = 0.333; $p \leq 0.018$ figure 3.3). There was no significant correlation among other parameters. (Table 5).

Table 1: Mean±SD values of demographic and serum measured biochemical Parameters of type 2 diabetic patients and healthy controls.

Parameter	Diabetic patients (N=50)	Controls (N=50)	*P-Value
Age (Year)	58.80±6.18	56.48±6.34	0.067
BMI (Kg/m^2)	26.99±4.72	25.21±3.03	0.027
Random serum glucose (mg/dl)	195.60±72.27	117.66±14.47	0.0001
Blood HbA1c %	9.16±2.53	4.95±0.42	0.0001
S. Magnesium (mg/dl)	1.61±0.38	1.95±0.24	0.0001

Table 2: Mean±SD values of serum magnesium and blood HbA1c of males and females of type 2 diabetic patients and healthy controls.

Parameter	T2DM Group (n=50)			Controls Group (n=50)		
	Males (N=28)	Females (N=22)	p- value	Males (N=25)	Females (N=25)	*P-Value
HbA1c %	9.11±2.20	9.23±2.95	0.882	4.968±0.457	4.936±0.397	0.793
Magnesium (mg/dl)	1.59±0.37	1.64±0.39	0.690	1.932±0.188	1.976±0.289	0.527

Table 3: Mean±SD values of serum magnesium levels in relation to BMI in type 2 diabetic patients.

Parameter	Normal weight T2DM (N=11)	Overweight T2DM (n=25)	Obese T2DM (n=14)
Magnesium (mg/dl)	1.60±0.402	1.76±0.38	1.36±0.19

Table 4: Mean±SD values of serum magnesium levels in relation to Glycemic Control in type 2 diabetic patients.

Parameter	HbA1c (< 7%) (N=16)	HbA1c (7 - < 8.5%) (N=10)	HbA1c (> 8.5%), (N=24)
Magnesium (mg/dl)	1.92±0.34	1.59±0.30•	1.42±0.29•

Table 5: Correlations among demographic and laboratory parameters of control group.

Correlations (Control)						
		age	BMI	Random serum glucose	HbA1c	Mg
Age	Pearson Correlation	1	.138	.089	.063	-.167
	Sig. (2-tailed)		.339	.538	.662	.247
	N	50	50	50	50	50
BMI	Pearson Correlation	.138	1	.363**	.333*	.099
	Sig. (2-tailed)	.339		.010	.018	.492
	N	50	50	50	50	50
Random serum glucose	Pearson Correlation	.089	.363**	1	.210	-.138
	Sig. (2-tailed)	.538	.010		.143	.338
	N	50	50	50	50	50
HbA1c	Pearson Correlation	.063	.333*	.210	1	-.097
	Sig. (2-tailed)	.662	.018	.143		.502
	N	50	50	50	50	50
Mg	Pearson Correlation	-.167	.099	-.138	-.097	1
	Sig. (2-tailed)	.247	.492	.338	.502	
	N	50	50	50	50	50

Discussion

The results of present study indicated that there was no significant difference in mean values of age between apparently healthy subjects and Type 2 diabetic patients, which is important to exclude age factor effect. The present study revealed significant increase in mean value of BMI in T2DM patients than in healthy controls. Bays *et al*. (2007) found the greater numbers of adults with diabetes mellitus were obese [10]. Gupta *et al* (2020) mentioned that insulin resistance take place due to increased discharge of lipids, fatty acids and other advancing factors due to presence of huge adipose tissue [11]. The current study found that significant difference in mean values of random serum glucose between diabetic patients and control groups. Patel *et al*. (2015) noticed that in a diabetic patients group, the mean postprandial blood glucose was more elevated than in healthy patient's group [12]. In recent time, significant attention has been focused on the postprandial state, since isolated postprandial hyperglycemia, as happen in persons with impaired glucose tolerance, has been shown to double the risk for death from cardiovascular disease and since postprandial hyperglycemia seem to be the rate-limiting factor for making optimal glycemic control in patients with type 2 diabetes. In people with type 2 diabetes, postprandial glucose liberate into the circulation is raised from endogenous and meal glucose due to increased glycogenolysis, elevated gluconeogenesis, and declined splanchnic glucose uptake, all of which are connected with abnormal insulin and glucagon secretion [13]. The present study found that there was no significant difference in the mean value of HbA1c between males and females in both patients and controls groups which is comparable to that obtained by Vadgama *et al*. (2021) [14]. However, a study of Alghamdi *et al*. (2020) noticed that the short lifespan of red blood cells that result from loss of blood through menstruation in the females before menopause is a possible reason for variations in the mean of HbA1c value between males and females that was significantly less in females than in men [15]. This discrepancy may reflect that both gender of the present study follow the same glycemic control and may also due to the limit number of the study cases. The study revealed significant decrease in serum magnesium level in obese T2DM patients compared with both overweight and normal weight T2DM patients. The same result obtained by Piuri *et al*. (2021) who mentioned that obesity and type 2 diabetes are blended conditions characterized by chronic low-grade inflammation somewhat attributable to magnesium deficiency. In metabolic diseases, a low magnesium situation mainly due to unhealthy food lead to create a pro-inflammatory condition that exacerbates metabolic derangement [16]. In addition, significant inverse correlations between serum magnesium levels and each of FBS, BMI, HbA1c were observed in diabetic patients of Babikr *et al*. (2016) study [17]. The present study was focused on the magnesium level in Type 2 diabetic patients and its relation with HbA1c and found significant difference in the mean value of serum magnesium levels between patients who had mean HbA1c value < 7 and those with HbA1c mean value (7- 8.5) as well as between patients who had HbA1c < 7 and those with HbA1c mean value > 8.5. These results agreed with Seedahmed *et al*. (2013) study who stated a significant drop in the mean value of the serum magnesium levels of diabetics group while their HbA_{1C} values were elevated [18]. A significant inverse correlation was documented between serum magnesium and age values of patients, which is agreed with other Mishra (2011) [19]. Magnesium deficiency in the old peoples can occur due to inadequate nutrient ingestion, many drug use like loop diuretics, immunosuppressive drugs, or changed gastrointestinal function [20]. There was also significant positive correlation between random serum glucose levels and the value of BMI in both diabetics and controls groups. These results come with those carried by Alghamdi *et al*. (2017) [21]. There was also significant direct correlation between HbA1c values and random serum glucose inT2DM patients group, the same result was founded by Absalome *et al*. (2020) [22]. The HbA1c value give though the average blood glucose level during the course of the red blood cells lifespan [23]. Importantly, the present study found significant negative correlations between serum magnesium levels and each of random serum glucose and the values of HbA1c in diabetics group. These results agreed with Kumar *et al*. (2019) study [24], Sobczak *et al*. (2019) study [25] and Seedahmed *et al*. (2013) study [26] but disagree with Saeed *et al*. (2019) who did not show such correlation [27]. Hereditary factors, poor dietary ingestion, autonomic dysfunction, changed insulin metabolism, glomerular over filtration, osmotic diuresis, frequent metabolic acidosis, hypophosphatemia and hypokalemia may all participate to hypomagnesaemia in diabetic patients [28].

Conclusions

- Iraqi type 2 diabetic patients suffered from significantly dropping in the blood magnesium level that is significant inverse correlated with blood glucose levels and HbA1c values.
- Obese and / or poor controlled diabetic patients are at high risk of developing magnesium deficiency.
- Magnesium deficiency in T2DM patients may be attributable agent of micro- and macro-vascular complications of DM.

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