# The level of serum magnesium activity in diabetes mellitus

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(Received 29 / 4 /2013 , Accepted 19 / 9 / 2013)

**الخلاصة:**
شملت الدراسة 96 شخصا مصابون بالسكر لفترة لاتقل عن خمسة سنوات و 95 شخصا اصحاء لايعانون من مرض السكر حيث انهم يمتلكون مسنوى سكر طبيعي في الدم وليس لهم تاريخ عائلي لهذا المرض، تم استخدامهم كمجموعة سيطرة. في هذه الدراسة، أجريت تحاليل المغنيسيوم والكرياتنين لكلا المجموعتين، وتحليل الهيموغلوبين السكري لمجموعة المرضى فقط ومن خلاله صنفت هذه المجموعة الى صنفين احدها منتظم السكر والاخرى غير منتظم السكر. أن قياس مستوى الكرياتنين لمعرفة اذا كان هنالك اي خلل كلوي قد يؤدي الى فقدان المغنيسيوم في الادرار وبالتالي التاثير على مستواه في الدم، حيث تم استبعاد هذه الحالات من الدراسة. بينت النتائج من هذه الدراسة ان هنالك نقصان معنوي عالي في مستوى المغنيسيوم في مصل المرضى مقارنة بمجموعة السيطرة. كذلك هنالك تاثير ايجابي لعملية تنظيم السكر على مستوى المغنيسيوم في دم المرضى. يمكن الاستنتاج من هذه الدراسة، ان نقص المغنيسيوم قد يضاف الى الاسباب الاخرى المسببة الى مرض السكر او قد يكون احد النتائج المتسببة منه.

## Abstract:
Objective: This study has been carried out to asses the activity of magnesium in the serum of patients with diabetes mellitus. Also the effect of glycemic control on magnesium levels was investigated.
Subjects and Methods: Ninety six patients with diabetes were enrolled in this study, together with 95 healthy subjects, matched for age and sex, who served as the control group. The serum levels of glucose, creatinine and magnesium were estimated in all subjects. Glycated hemoglobin (HbA1c) was estimated in diabetic patients and according to its level we classified the diabetic into 2 groups: Group 1: good glycemic control (57 patients). Group 2: poor glycemic control (39 patients).
Results: Serum magnesium levels in diabetic group were found to be significantly lowered than in control group. We found a direct correlation between the Glycosylated hemoglobin and magnesium levels in our study.
Conclusion: The present study revealed that there is inverse relationship between the magnesium levels and the glucose homeostasis in diabetic patients. Furthermore, there is an affirmative effect for the glycemic control on the level of magnesium in diabetic patients.

## Introduction:
Diabetes mellitus, often referred simply as diabetes (Ancient Greek: "to pass through"), is a syndrome of disordered metabolism, resulting in abnormally high blood sugar levels (Hyperglycemia). A deficiency of insulin or a resistance to its action is responsible for the abnormalities [(1)]. Diabetes is world-wide in distribution and the incidence of both types is rising. However, the prevalence of both varies considerably in different parts of the world and this is probably due to differences in genetic and environmental factors [(2)].

A person can be in the pre-diabetic state for as long as ten years without exhibiting any signs or symptoms of diabetes [(3)]. Although no overt signs or symptoms may be seen, these pre-diabetic patients will have started developing macrovascular and microvascular complications [(4)].

The cause of diabetes incidence is multi-factorial, recent evidence suggests that certain foods and dietary factors may be associated with this disease. In particular, high consumption of whole grains, beans, nuts, fruits and vegetables has been related to a reduced risk of type 2 diabetes mellitus [5]. These foods are rich sources of magnesium, a trace mineral involved in over 300 enzymatic reactions in the body [6]. It plays a fundamental role as a cofactor in various enzymatic reactions involving energy metabolism. The almost universal involvement of magnesium in a wide variety of cellular processes critical to glucose metabolism, insulin action and cardiovascular functions has been well appreciated [7]. It is a cofactor in the glucose-transporting mechanism of the cell membrane and various enzymes in carbohydrate oxidation. It is also involved at multiple levels in insulin secretion, binding and activity [8].

Several studies found that Magnesium deficiency (hypomagnesaemia) is a contributing factor in diabetes and the development of diabetic complications [9,10]. A significant relationship between magnesium and whole-body glucose homeostasis and insulin sensitivity has been demonstrated [11], Low levels of magnesium increase the development of insulin resistance and alter the ability of cells to take up glucose [12]. Dietary magnesium has also been found to be protective against the development of diabetes [13].

In the present study, serum level of magnesium was measured in patients with diabetes and the influence of control of diabetes on serum concentration of this element was determined. The primary aim was to ascertain whether or not patients with diabetes had a magnesium deficiency, as magnesium has been implicated in the pathogenesis of insulin resistance.

## Materials and Methods:

### Subjects:

This cross-sectional study was conducted in the period from January to June 2011 in our outpatient diabetic clinic. A total of 96 diabetic patients with duration of disease at least five years (53 males and 43 females) with ages varied from 24-70 years were labeled as diabetic group. Ninety five healthy (with normal fasting blood sugar test), sex and age matched subjects with no family history of diabetes were labeled as control group. Patients with previous nephropathy, plasma creatinine > 2 mg/dl were excluded from the study.

In order to study the effect of uncontrolled diabetes on the magnesium levels, the diabetic patients were further subdivided into two groups. Group I had 57 controlled patients with a glycated hemoglobin (HbA1c) level less than or equal to 7% of total hemoglobin (Hb). Group II had 39 uncontrolled diabetic patients with HbA1c levels of more than 7% of total Hb.

Blood sample collection:

About 5 ml of venous blood were obtained from all subjects after an overnight fast. Samples were analyzed for glucose, Magnesium, and Creatinine. Glycated hemoglobin (HbA1c) was measured in the diabetic group to diagnose their glycemic control.

Magnesium measurement:

The serum was investigated for magnesium immediately by using human diagnostic kit depending on photometric colorimetric test for magnesium with lipid clearing factor (LCF). In this method, the magnesium in an alkaline medium forms a colored complex with

xylidyl blue, which has an absorbance peak at 520 nm [14].

Glucose assay:

The glucose assay was performed based on colorimetric enzyme method. In this method, glucose with effect of glucose oxidase can be enzymatically oxidized to gluconic acid and hydrogen peroxide in the presence of peroxidase, the hydrogen peroxide reacts with 4-amine antipyrine (4-AAP) and N-ethyl-N-sulfopropyl-m-toludine (TOPS) to form violet-colored quinoneimine, which has an absorbance peak at 520nm [15].

Glycated hemoglobin measurement:

Glycosylated hemoglobin (HbA1c) was measured using the thiobarbituric acid colorimetric reaction. The colorimetric method with 2-thiobarbituric acid is based on the hydrolysis of the glycated proteins using oxalic acid at 100$^{o}$c yielding 5- hydroxy methyl furfural (5-HMF) which react with thiobarbituric acid. The absorbance measured at 443nm. 5-HMF was used as a standard and glycation of hemoglobin [16].

Creatinine assay:

The serum was investigated for creatinine by using sigma diagnostic kit. The method depend on that creatinine reacts with picric acid under alkaline conditions to form a yellow-orange complex. The color is derived from creatinine as well as certain other non-specific substances. Upon the addition of acid, the color contributed by creatinine is destroyed, while that produced by non-specific substances remains. The difference in color intensity measured at 500 nm before and after acidification is proportional to the creatinine concentration [17].

Statistical analysis:

The data collected will be tabulated and analyzed using mean, standard deviation, and comparison between the groups by using p-value analysis. Complete analysis will be carried out using SPSS package.

## Results:

Table 1 shows the age and sex of diabetic and non-diabetic subjects in the study. The distribution shows that the diabetes was more in the subjects with ages more than forty (64%) and also it is more in male than female 55% to 45% respectively.

**Table1 the distribution of diabetic and nondiabetics subjects participated in the study**

| Variables | | Cases(n=96) | | Controls(n=95) | | Total(n=191) | |
|---|---|---|---|---|---|---|---|
| | | No. | % | No. | % | No. | % |
| Age (years) | ≤ 40 | 34 | 36 | 36 | 38 | 70 | 37 |
| | > 40 | 62 | 64 | 59 | 62 | 121 | 63 |
| Sex | Male | 55 | 55 | 57 | 60 | 112 | 58 |
| | Female | 41 | 45 | 38 | 40 | 81 | 42 |

The results of magnesium activity in diabetic patients and healthy control subjects are shown in table 2. In diabetic group, the magnesium activity was 1.0 – 2.10 mg/dl, while that of control group was 1.80 – 2.60 mg/dl.

The differences in magnesium activity between the two groups were statistically highly significant ($p<0.001$). In 8.3 % of the diabetic patients the magnesium concentrations were up the reference range of 1.9-2.5 mg/dl.

**Table 2 Magnesium activity in diabetic patients and healthy control subjects.**

| Serum magnesium | Cases | Control |
|---|---|---|
| Range (min-max) | 1.0 – 2.10 | 1.80 – 2.60 |
| Mean ± SD | 1.67 ± 0.37 | 2.03 ± 0.25 |
| 95 % CI | 0.052 – 1.56 | 0.04 – 1.90 |
| Significance | Highly significant | |

Table 3 Shows the serum magnesium levels in diabetic with good glycemic control (HbA1c ≤ 7%) and those with poor glycemic control (HbA1c > 7%). The magnesium levels were significantly higher in diabetics with good glycemic controls than those with poor glycemic controls. Significant difference was observed in the serum magnesium levels of both groups.

**Table 3 Comparison magnesium levels between good and poorly glycemic groups.**

| Serum magnesium (mg/dl) | Good glycemic control HbA1c ≤ 7% | Poorly glycemic control HbA1c > 7% |
|---|---|---|
| Range (min-max) | 1.20 – 2.50 | 1.00 – 1.60 |
| Mean ± SD | 1.75 ± 0.34 | 1.25 ± 0.19 |
| 95 % CI | 1.64 – 1.85 | 1.09 – 1.40 |
| Significance | Significant | |

## Discussion:

In our study, we observed decreased in serum magnesium levels in diabetic patients. , this finding is in agreement with those of other studies [18,19,20]. Although we determined creatinine levels in our patients, this additional factor to consumed if there is a hypomagnesaemia according to renal dysfunction.

Magnesium is known to play an important role in carbohydrate metabolism, and its imbalance has been implicated in diabetes mellitus both as a cause and a consequence [21].

Magnesium is a key element in cellular metabolism, and its involvement in critical enzymes systems within the body is extensive. As an intracellular element, magnesium is needed for the activation of hexo-kinase, which is required in the conversion of glucose to glucose-6-phosphate. This is the first step in the glycolysis cycle involving carbohydrate metabolism. The requirement for magnesium continues into and through the function of the Krebs cycle and is involved in the conversion of pyruvate to coenzyme A. It is an important requirement for normal functioning of both anaerobic and aerobic metabolism.[22]

Cellular magnesium deficiency can alter the activity of membrane bound $Na^+$-$K^+$ ATPase which is involved in maintenance of gradients of $Na^+$, $K^+$ and in glucose transport [23].

The utilization of glucose by peripheral tissues is dependent on insulin. Serum magnesium levels have been shown to influence the secretion, binding and activity of insulin [24]. In fact, it has been shown that there is a direct relationship between serum magnesium level and cellular glucose utilization related to increase sensitivity of tissues to insulin [25].

Hypomagnesaemia may be a consequence for diabetes; increase urinary loss of magnesium may contribute to it. Two factors may work together in this respect, namely, the osmotic action of glucosuria as well as hyperglycemia per se, the latter being known to depress the net tubular resorption of magnesium in normal man [26].

Glycosylated Haemoglobin (HbA1c) results from post translational changes in the haemoglobin molecule, and their levels correlate well with glycemic levels over the previous six to ten weeks. Glycosylation of haemoglobin takes place under physiological condition by a reaction between glucose and N terminal valine of Beta chain of Hb molecules [27].

We measured HbA1c levels in our diabetic patients to know the status of magnesium in the good and poor glycemic control. We found a significantly higher magnesium levels in the well glycemic control compared to the poor glycemic control.

From our observations, we therefore conclude that diabetes and poor glycemic control alters the metabolism magnesium by causing hypermagnesuria.

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