# Serum magnesium in children with type 1 diabetes and its correlation to glycemic control

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**Abstract: Background:** Type 1 diabetes mellitus (T1DM) is highly prevalent endocrinal disorder. with incidence of around 8/100,000 per year in Egyptian children under the age of 15 years. Evidence indicate that Magnesium (Mg) plays an important role in prevalence of T1DM. and its complications. Thus we aimed to find out the effect of T1DM. on serum Mg level. **Methods:** We included 50 Egyptian children with type 1diabetes at Pediatric outpatient clinic, Al-Hussein University Hospital and El-Sahel Teaching Hospital, and 25 age- and sex-matched healthy individuals in a case-control study. We measured Serum magnesium, HbA1c, random blood suger, serum urea, and creatinine level and CBC. **Results:** Diabetic children had significantly lower serum magnesium level compared to control children (1.91 ± 0.22 mg/dL in diabetic children versus 2.08 ± 0.19 mg/dL in control children). Hypomagnesemia was detected in 26% of diabetic children compared to 8% of control children. Significant negative correlation between serum Mg and HbA1c was detected. ($p_{=}$0.000 $r_{=}$-0.703). also negative correlations between Mg and each of age and duration of DM. ($p_{=}$0.016; $r_{=}$-0.339); (p=0.000; $r_{=}$-0.339) respectively. **Conclusion:** patients with T1DM more liable to develop hypomagnesemia specially with poor glycemic control.
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## 1. Introduction

Type 1 diabetes mellitus (T1DM) is one of the most common endocrine and metabolic conditions in childhood. ]1[Type 1 diabetes is generally thought to be precipitated by an immune-associated, if not directly immune-mediated, destruction of insulin-producing pancreatic β cells.]2[

Data from large epidemiological studies worldwide indicate that on an annual basis, the overall increase in the incidence of T1DM is around 3% and about 78,000 children under age 15 years develop T1DM worldwide. The worldwide geographic variation in the incidence of T1DM is striking. Among Eastern Mediterranean and Middle Eastern countries, the largest contribution to the total number of estimated childhood T1DM cases comes from Egypt which accounts for about a quarter of the region's total. The incidence varies between 1/100,000 per year (Pakistan) and 8/100,000 per year (Egypt) in children under the age of 15 years.]1[

Mg plays an important role in whole reactions, including cellular energy transfer, glycolysis and phosphorylation, and it prevents free radical generation required to ensure increased glutathione syntheses. ]3[Moreover, Mg deficiency is involved in the pathogenesis of diabetes complications that inhibit the prostacyclin receptor function and cause increased thrombocyte activation and aggregation. ]4[

Numerous causes for low magnesium levels in diabetics can be listed including diets low in magnesium, osmotic diuresis that leads to high renal excretion of magnesium, insensitivity to insulin that affects intracellular magnesium transport and causes increased loss of extracellular magnesium, usage of loop and thiazide diuretics that promote magnesium wasting, diabetic autonomic neuropathies, and reduced tubular reabsorption due to insulin resistance. Additionally, continuous magnesium deficiency correlates to higher levels of TNFα, which may also contribute to post-receptor insulin resistance. ]5[

## 2. Patients and Methods

This case control study was carried out on children and adolescents patients at Al-Hussein University Hospital and Al Sahel Teaching Hospital from May, 2017 to October, 2017 according to inclusion and exclusion criteria blow. Another group of age- and sex-matched healthy individuals with no obvious medical disorders and not receiving any medication were enrolled as a control group.

**Inclusion criteria:**

1. Type 1 diabetes.
2. Age between 1 and 18 years.
3. Duration since onset of DM at least 6 months.

**Exclusion criteria:**

1. Children who have renal disease detected by serum urea and creatinine test.
2. Children with persistent diarrhea and vomiting.
3. Type 2 diabetes.

4. Patients receiving medication affacting Mg.

**Study groups:**

1. Patient group: 50 children with type I diabetes.
2. Control group:25 age- and sex-matched healthy subjects recruited form community.

**Methods:**

All subjects underwent the following:

1. Thorough history taking and complete physical examination.
2. Investigations: complete blood count, renal function tests, random blood glucose, glycosylated hemoglobin, and serum magnesium.

**Ethical consideration:**

An informed written consent was obtained from each patient or control or their legal guardians before enrollment in the study. This study was approved from the local ethical committee of Al-Azhar University.

**Statistical analysis:**

Data were collected, revised, coded and entered to the Statistical Package for Social Science (IBM SPSS) version 23. The quantitative data were presented as mean, standard deviations and ranges when their distribution found parametric. Also qualitative variables were presented as number and percentages. The comparison between groups with qualitative data were done by using Chi-square test and Fisher exact test instead of the Chi-square only when the expected count in any cell found less than 5.

The comparison between two groups with quantitative data and parametric distribution were done by using Independent t-test. The comparison between more than two independent groups with quantitative data and parametric distribution was done by using One Way Analysis of Variance (ANOVA).

Spearman correlation coefficients were used to assess the correlation between two quantitative parameters in the same group. Uni-variate and Multi-variate regression analysis was used to assess predictors of Mg level in patients group. The confidence interval was set to 95% and the margin of error accepted was set to 5%. So, the p-value was considered significant as the following:

$P > 0.05$: Non significant

$P < 0.05$: Significant

$P < 0.01$: Highly significant.

**3. Results**

The study included 50 type 1 diabetic patients; 24 males and 26 females. They were compared to 25 age- and sex-matched healthy subjects served as controls. The control group consisted of 13 males and 12 females. The mean age of patients was 9.02 ± 3.06 years (range, 3 – 15 years) while that of controls was 9.60 ± 3.81 years (range, 3 – 15 years). The mean duration of disease in patient group was 4.02 ± 2.03 (range, 1 – 9 years). Table 1

Taking the cut off level of serum magnesium < 1.7 mg/dl. for definition of hypomagnemia., it was found that, hypomagnesemia was detected in 26% of patient group (13 of 50 )., compared to 8% in control group (2 of 25). There was significant difference between the mean Mg level in patient group 1.91 ± 0.22 (range, 1.55 – 2.38), compared to 2.08 ± 0.19 (range, 1.61 – 2.33) in control group. Also, significant difference between the mean HbA1c level in patient group 9.09 ± 1.68 (range, 5.9 – 13.5), compared to 5.72 ± 0.31 (range, 5 – 6.2) in control group was detected. There was significant difference in mean random blood suger in patient group 150.02 ± 44.24 (range, 87 – 271), compared to 119.24 ± 28.81 (range, 79 – 167) in control group. Table 2

In patient group, significant negative correlations between Mg and age, duration of DM, HBA1c and RBS were detected. Table 3

By dividing study group into 4 quartiles based on serum Mg level, First quartile (Q1), serum Mg level < 1.67; Second quartile (Q2), serum Mg level 1.67-1.93; Third quartile (Q3), serum Mg level 1.97-2.02; Fourth quartile (Q4), serum Mg level > 2.02; It was detected that, Q1 (which had lowest Mg level) had longest duration of DM (mean 5.95 ± 2.49), and the highest level of HbA1c (mean 10.98 ± 1.45). highly significant correlation was found. Table 4

In Uni-variate analysis for predictors of Mg level in patients group, each single variant had independent effect on serum Mg level. Table 5. In Multi-variate analysis for predictors of Mg level in patients group, HbA1c had most significant effect on serum Mg level. Table 6

**Table 1: Mean age and duration of DM in study groups.**

| | | Control group | Patients group | Independent t-test | |
|---|---|---|---|---|---|
| | | No. = 25 | No. = 50 | t | p-value |
| Age (yrs) | Mean±SD | 9.60 ± 3.81 | 9.02 ± 3.06 | 0.712 | 0.479 |
| | Range | 3 – 15 | 3 – 15 | | |
| Duration of DM | Mean±SD | - | 4.02 ± 2.03 | - | - |
| | Range | - | 1 – 9 | | |

| Table 2: Mean Mg level, HbA1c and RBS in study groups. | | | | | |
|---|---|---|---|---|---|
| | | Control group | Patients group | Independent t-test | |
| | | No. = 25 | No. = 50 | T | p-value |
| Mg | Mean±SD | 2.08 ± 0.19 | 1.91 ± 0.22 | 3.252 | 0.002 |
| | Range | 1.61 – 2.33 | 1.55 – 2.38 | | |
| HbA1c | Mean±SD | 5.72 ± 0.31 | 9.09 ± 1.68 | -9.925 | 0.000 |
| | Range | 5 – 6.2 | 5.9 – 13.5 | | |
| RBS | Mean±SD | 119.24 ± 28.81 | 150.02 ± 44.24 | -3.154 | 0.002 |
| | Range | 79 – 167 | 87 – 271 | | |

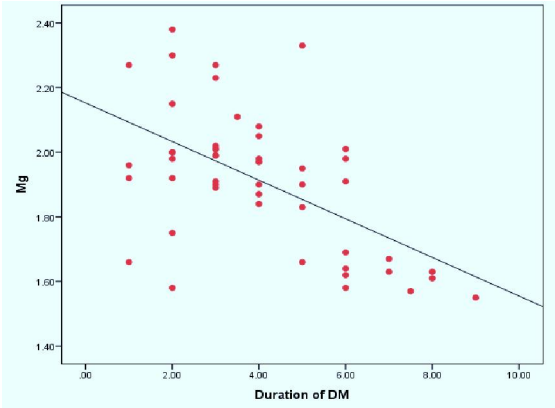


**Fig.1: Negative correlation of Mg level with duration of DM.**

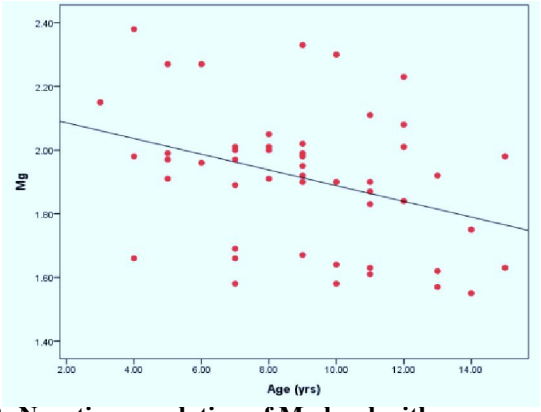


**Fig.2: Negativecorrelation of Mg level with age.**

| Table 3: Correlation of Mg level with the other studied parameters. | | |
|---|---|---|
| | Mg | |
| | r | p-value |
| Age (yrs) | -0.339* | 0.016 |
| Duration of DM | -0.501** | 0.000 |
| HbA1c | -0.703** | 0.000 |
| RBS | -0.338* | 0.016 |
| Urea | -0.478** | 0.000 |
| Creat | -0.370** | 0.008 |

| Table 4: Comparison of serum magnesium concentration quartiles as regard laboratory findings. | | | | | | | |
|---|---|---|---|---|---|---|---|
| | | First quartile | Second quartile | Third quartile | Fourth quartile | One Way ANOVA | |
| | | | | | | F | P-value |
| Age (yrs) | Mean±SD | 10.45 ± 3.36 | 9.71 ± 2.49 | 8.00 ± 2.80 | 8.00 ± 3.33 | 2.105 | 0.113 |
| | Range | 4 – 15 | 5 – 14 | 4 – 15 | 3 – 12 | | |
| Duration of DM | Mean±SD | 5.95 ± 2.49 | 3.93 ± 1.73 | 3.40 ± 1.45 | 2.95 ± 1.21 | 6.230 | 0.001 |
| | Range | 1 – 9 | 1 – 7 | 1 – 6 | 1 – 5 | | |
| HbA1c | Mean±SD | 10.98 ± 1.45 | 9.02 ± 1.52 | 8.55 ± 1.29 | 7.93 ± 0.83 | 10.929 | 0.000 |
| | Range | 8.4 – 13.5 | 7.2 – 12 | 7 – 11.6 | 5.9 – 9.2 | | |
| RBS | Mean±SD | 179.45 ± 46.26 | 144.79 ± 50.11 | 142.07 ± 40.14 | 136.90 ± 27.34 | 2.315 | 0.088 |
| | Range | 97 – 241 | 93 – 271 | 89 – 221 | 87 – 167 | | |
| Urea | Mean±SD | 37.00 ± 2.90 | 30.43 ± 2.93 | 30.40 ± 3.54 | 29.80 ± 4.37 | 11.105 | 0.000 |
| | Range | 31 – 40 | 27 – 37 | 25 – 36 | 22 – 38 | | |
| Creat | Mean±SD | 1.08 ± 0.11 | 0.88 ± 0.10 | 0.86 ± 0.12 | 0.91 ± 0.15 | 8.403 | 0.000 |
| | Range | 0.9 – 1.2 | 0.68 – 1 | 0.65 – 1.05 | 0.65 – 1.2 | | |

| Table 5: Uni-variate analysis for predictors of Mg level in patients group. | | | | | |
|---|---|---|---|---|---|
| | Unstandardized Coefficients | | Standardized Coefficients | t | P-value |
| | B | Std. Error | Beta | | |
| Age (yrs) | -0.025 | 0.010 | -0.349 | -2.584 | 0.013 |
| Duration of DM | -0.060 | 0.013 | -0.562 | -4.706 | 0.000 |
| HbA1c | -0.091 | 0.013 | -0.705 | -6.896 | 0.000 |
| RBS | -0.002 | 0.001 | -0.382 | -2.867 | 0.006 |
| Urea | -0.025 | 0.006 | -0.500 | -3.995 | 0.000 |
| Creat | -0.556 | 0.204 | -0.365 | -2.719 | 0.009 |

| Table 6: Multivariate analysis for predictors of Mg level in patients group. | | | | | |
|---|---|---|---|---|---|
| | Unstandardized Coefficients | | Standardized Coefficients | t | P-value |
| | B | SE | Beta | | |
| (Constant) | 2.854 | 0.167 | | 17.072 | 0.000 |
| Age (yrs) | -0.001 | 0.008 | -0.017 | -0.144 | 0.886 |
| Duration of DM | -0.020 | 0.014 | -0.189 | -1.399 | 0.169 |
| **HbA1c** | **-0.059** | **0.017** | **-0.460** | **-3.391** | **0.002** |
| RBS | -0.001 | 0.001 | -0.198 | -1.761 | 0.085 |
| Urea | -0.019 | 0.011 | -0.386 | -1.678 | 0.101 |
| Creat | 0.477 | 0.331 | 0.314 | 1.441 | 0.157 |

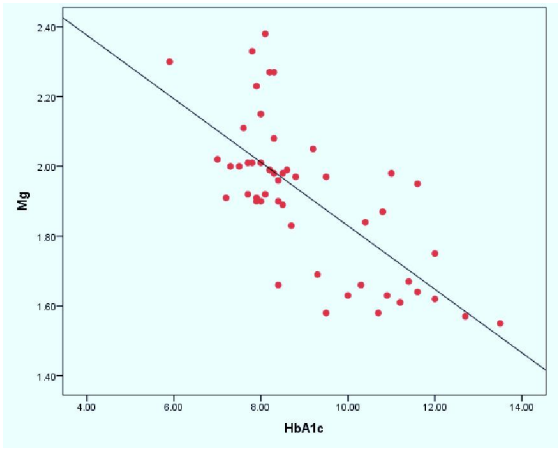


**Fig. 3: Negativecorrelation of Mg level with HbA1c**.

**Discussion**

The incidence of T1DM is increasing worldwide and it is estimated that nearly 90,000 children are diagnosed each year. ]6[Magnesium plays a central role as a cofactor in many enzymatic reactions involved in energy production. It is essential for both the manufacture and action of insulin, and can inhibit insulin secretion and activate insulin receptor tyrosine kinase activity.]7[

In this study, we found statistically significant difference in percentage of hypomagnesemia between diabetic patients and control group being higher in diabetic group, as percentage was 26 % in the diabetic group versus 8 % in the control group with lower level of serum magnesium in patients (Mean±SD 1.91 ± 0.22 mg/dL) versus (Mean±SD 2.08 ± 0.19 mg/dL) in control children.

These results are in concordance with ***Khubchandani AS, and Sanghani H, 2013.,***]8[ on study conducted in BJ Medical College and Civil Hospital, Ahmed abad with 75 subjects (50 patients with diabetes and 25 normal healthy controls), that revealed a lower serum magnesium level in diabetic children compared to control subjects. In an other study on the patients lived in the Northeast areas of China***, Xu J, et al, 2013.,***]9[ found lower serum magnesium level in diabetic patients compared to control subjects.

Also, ***Galli-Tsinopoulou A, et al, 2014.,***]10[In cross-sectional study on 138 children and adolescents with T1DM aged between 1.9 and 20.3 years (61 children, 77 adolescents; 72 boys, 66 girls) who were followed-up in the Outpatient Unit of the 4th Department of Pediatrics, Faculty of Medicine, Aristotle University of Thessaloniki, found 25% of patients had hypomagnesemia.

In our study, we detected significant negative correlation between serum Mg level and HbA1c. By dividing study subjects to 4 quartiles based on the serum magnesium level, we found that Q 1 with the lowest serum magnesium level was associated with longer duration of diabetes, higher HbA1c, and poor glycemic control versus other quartiles with higher serum magnesium. We observed also a negative correlation between serum magnesium level and HbA1c. This agreed with ***Galli-Tsinopoulou A, et al,2014.,***]10[sudy on type I diabetic children that

showed a lower Mg level in patients with poor glycemic control with high HbA1c.

Also, ***Ramadass S, et al,2015.,***]11[in study on 50 patients of Diabetes Mellitus type 2 attending the clinics or admitted in the wards of a tertiary care centre in Puducherry, South India., found that Magnesium levels decrease with increase in the duration of Diabetes Mellitus, and revealed a strong negative correlation between Mg and HbA1c.

Inconsistent with our result, ***Matthiesen G, et al,2004.,***]12[study on 81 Danish children with type 1 diabetes, did not show any correlation between serum magnesium level and HbA1c in type 1 diabetic children and adolescents this difference between these studies and ours could be attributed to short duration of DM., the difference in study populations, also to the different methods of evaluating serum magnesium and glycemic control.

**Conclusion**

From this study we conclude that, hypomagnesemia is more common in T1DM patient than healthy control subject, Age, and duration of DM have negative effect on serum Mg level, and there is negative correlation between serum Mg and HbA1c reflecting that " incidence of hypomagnesemia increases with poor glycemic control ". We suggest regular monitoring of serum magnesium in children with type 1 diabetes and correcting hypomagnesemia if present. We need to perform further studies on giving magnesium supplements in diabetic children with hypomagnesemia to observe the effect of correction of serum magnesium on glycemic control, lipid profile, and the risk of diabetic complications.

**References**


1. El-Ziny MA, Salem NA, El-Hawary AK, Chalaby NM, Elsharkawy AA.: Epidemiology of Childhood Type 1 Diabetes Mellitus in Nile Delta, Northern Egypt - A Retrospective Study. Journal of Clinical Research in Pediatric Endocrinology. 2014;6(1):9-15.
2. Todd JA.: Etiology of type 1 diabetes. Immunity. 2010; 32:457–67.
3. Salmonowicz B, Krzystek-Korpacka M, Noczyńska A.: Trace elements, magnesium, and the efficacy of antioxidant systems in children with type 1 diabetes mellitus and in their siblings. Adv Clin Exp Med. 2014;23:259–268.
4. Nadler JL, Rude RK,: Disorders of magnesium metabolism. Endocrinol Metab Clin North Am. 1995;24:623–641.
5. Dasgupta A, Sarma D, Saikia UK.: Hypomagnesemia in type 2 diabetes mellitus. Indian J Endocrinol Metab2012;16:1000–3.
6. Diaz-Valencia PA, Bougneres P & Valleron AJ.: Global epidemiology of type 1 diabetes in young adults and adults: a systematic review. BMC Public Health (2015)15, 255.
7. Lin CC, Tsweng GL, Lee Ch F, Chen BH, Huang YL,: Magnesium, zinc, and chromium levels in children, adolescents, and young adults with type 1 diabetes, Clinical Nutrition (2015): 1-5.
8. Khubchandani AS, and Sanghani H,: Study of Serum Magnesium and Hb A1C in Diabetic Patients along with Changes in their Lipid Profiles Indian Journal of Clinical Practice, April 2013. Vol. 23, No. 11, 717-719.
9. Xu J, Xu W, Yao H, Sun W, Zhou Q.: Associations of Serum and Urinary Magnesium with the Pre-Diabetes, Diabetes and Diabetic Complications in the Chinese Northeast Population. PLoS ONE (2013) 8(2): e56750.
10. Galli-Tsinopoulou A, Maggana I, Kyrgios I, Mouzaki K, Grammatikopoulou MG, Stylianou C, Karavanaki K,: Association between magnesium concentration and HbA1c in children and adolescents with type 1 diabetes mellitus. J Diabetes. 2014;6:369–377.
11. Ramadass S, Basu S, Srinivasan AR.: Serum magnesium levels as an indicator of status of Diabetes Mellitus type 2. Diabetes Metab Syndr. 2015;9(1):42-5.
12. Matthiesen G, Olofsson K, Rudnicki M,: Ionized Magnesium in Danish Children With Type 1 Diabetes. DIABETES CARE, MAY 2004:27, 5,.1216-1217.
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