

STATUS OF SERUM MAGNESIUM IN CHILDREN WITH TYPE 1 DIABETES MELLITUS: RELATION TO GLYCEMIC CONTROL

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ABSTRACT

Background: Magnesium has an important role in the metabolism of carbohydrate so that it may affect the release and activation of insulin which is the hormone that controls levels of blood glucose. Different studies all over the world have found a low serum Magnesium in diabetic children with poor glycemic control reflected mainly by glycated hemoglobin (HbA1c) level. Our aim was to evaluate the serum magnesium status in children with type 1 diabetes and to assess its relation to glycemic control.

Methods: A case control study included 50 diabetic patients whose ages were between 1 and 18 years and 50 controls who were age- and sex-matched chosen from the siblings of the patients who visited the center during the study period. Serum Magnesium was assayed and acut off point equal to and above 1.7 mg/dl considered as normal level. The glycemic control of patients was classified according to HbA1c % as good <7.5%, poor 7.5-8.5% and very poor >8.5%. Data were statistically analyzed using SPSS 22. A P value of <0.05 was considered significant.

Results: of the total patients 32% had Hypomagnesemia compared to 10% of controls. Serum magnesium level was significantly lower in diabetic children as compared to controls ($p < 0.007$). The diabetic patients in the first quartile had the lower value of serum magnesium. The remaining values, including duration of diabetes and HbA1 were comparably non-significant. A significant inverse correlation was found between serum magnesium and glycated hemoglobin level ($r = -0.302$, $p = 0.033$).

Conclusion: Serum magnesium level is frequently low in children with type 1 diabetes mellitus. There is a significant correlation between serum magnesium level and the glycemic control. Therefore we recommend doing regular monitoring of serum magnesium in type 1 diabetic children and appropriate supplement of low levels.

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Keywords: Magnesium, diabetes, HbA1c, glycemic control, hypomagnesemia

Diabetes mellitus is accompanied by alteration in the metabolism of micronutrients and magnesium (Mg) is the most common one studied in this regard. Mg has an important role in the metabolism of carbohydrate so that it may affect the release and activation of insulin which is the hormone that controls levels of blood glucose¹.

Mg is the fourth most abundant cation in the body and its biggest portion is stored in the cells. The magnesium homeostasis is mostly under the control of major organs; gut, kidney and sbonebut it is not yet fully understood what regulators affect these organs at the cellular level².

Magnesium has a widespreadrolein the body. More than 300 enzymes depend on it

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as an essential cofactor including those playing role in synthesis of carbohydrates, lipid, proteins, and nucleic acids, glycolysis, neuromuscular transmission, transcellular ion transport and the release of end response to certain hormones³.

Mg is involved in ATP use, ion channels, cell membrane and mitochondrial function. Moreover, hypomagnesemia may secondarily induce hypocalcemia, hypokalemia and hypophosphatemia that potentially cause more derangements in the physiology of neuromuscular and cardiovascular systems. Low serum Mg levels have been implicated in various long-term complications of diabetes mellitus like hypertension, coronary artery disease, increased thickness of carotid wall, ischemic stroke, dyslipidemia, diabetic neuropathy, retinopathy, and foot ulcerations⁴. Hypomagnesaemia also plays part in diabetic nephropathy. Hypomagnesaemia has been proposed to be a predictor of end-stage renal disease in diabetic nephropathy⁵. Moreover; magnesium deficit leads to carbohydrate intolerance and insulin resistance and thereby induces or worsens diabetes mellitus⁶.

Different studies all over the world have found a lower serum Mg in type 1 diabetic children with poor glycemic control reflected mainly by HbA1C level as compared to their healthy age- and sex-matched controls⁷⁻⁹.

Several studies were focused on evaluating Mg status in patients with type 2 diabetes and the role of supplementation of Mg to prevent diabetic complications and to optimize the diabetic control. A few studies have been concerned with serum Mg level in children with type 1 diabetes

with opposing results. Our aim was to evaluate the serum Mg status in Kurdish children with type 1 diabetes in Duhok and to assess its relation to glycemic control.

PATIENTS AND METHODS

A case control study was conducted at Azadi Diabetes Center in Duhok city/north of Iraq from 1st of September 2017 to 1st of September 2018. The study included 50 diabetic patients whose ages were between 1 and 18 years. Patients on diuretics, had diarrhea and or vomiting or renal impairment were excluded. Fifty controls who were age and sex-matched were included. They were chosen from the siblings of the patients who visited the center during the study period.

Serum Magnesium measurement was done by Integra 400 Plus (Roche, Germany). A serum Magnesium cut off equal to and above 1.7 mg/dl was considered as normal level. Complete blood count included Hemoglobin A1c level (HbA1c), Hemoglobin (Hb), Mean cell volume (MCV), White blood cells (WBC), Neutrophil count and Lymphocyte count. The glycemic control of patients was classified according to HbA1c % as good <7.5%, poor 7.5-8.5% and very poor >8.5%. The results were expressed as mean±SD. Data were statistically analyzed using SPSS 22. Differences between groups were assessed by paired Student's t test. Correlation between variables was assessed using Spearman rank correlation coefficient. A P value of <0.05 was considered significant. Ethical approval was taken from the Ethical Committee at The General Directorate of Health in Duhok.

RESULTS

The study included 50 patients (26 males and 24 females) whose mean age was 11.82 ± 3.89 years and 50 controls (29 males and 21 females) whose mean age was 10.89 ± 0.50 years. Serum magnesium level was significantly lower compared to controls as in Table 1.

Taking cut off of serum magnesium <1.7 mg/dL for definition of hypomagnesemia, 10 hypomagnesemia was detected in 32% of patients compared to 10% of controls.

Table 1: Comparison between Diabetic Patients and Controls as Regard Serum Magnesium Level

Serum Mg	Cases(n=50)	Controls(n=50)	P value
Mean \pm SD	1.83(+/-0.432)	1.91(+/-0.19 \pm)	
Serum Mg <1.7 mg/dl	16(32%)	5 (10%)	0.007
Serum Mg ≥ 1.7 mg/dl	34(68%)	45(90%)	

Patients were divided into 4 quartiles based on serum magnesium level: Q1 (serum magnesium <1.67 mg/dL); Q2 (serum magnesium 1.67 – <1.93 mg/dL); Q3 (serum magnesium 1.93 – 2.02) and Q4 (serum magnesium >2.02). We found that

patients in the first quartile had the lowest value of serum Mg but no significant differences were detected in relation to the duration of diabetes mellitus, mean HbA1c and the glycemic control.

Table 2: Comparison of Serum Magnesium Concentration Quartiles as Regard Clinical and Laboratory Findings in Diabetic Patients

	Mg < 1.67	Mg 1.67 — <1.93	Mg 1.93 - 2.02	Mg >2.02	P value
Serum Mg(mg/dl)					ANOVA
Mean	1.46	1.82	2	2.4	<0.001
SD	0.24	0.08	0	0.61	
Duration of DM(Years)					ANOVA
Mean	5	4.2	4.2	3.05	0.348
SD	2.50	2.54	3.11	2.29	
Hb A1C (%)					ANOVA
Mean	11.29	10.30	8.9	9.38	0.083
SD	2.53	2.28	1.31	1.21	
Glycemic control(HbA1C)					Fisher's Exact test
Good <7.5	1(6.3%)	2(10%)	0(0%)	0(0%)	
Poor 7.5 - 8.5	2(12.5%)	2(10%)	2(40%)	3(33%)	0.53
Very poor >8.5	13(81.3%)	16(80%)	3(60%)	6(66.7%)	

The level of HbA1c is significantly affected by the age of the diabetic patients while none of gender, duration of diabetes

or serum magnesium has a significant effect as in table 3.

Table 3: Multivariate Linear Regression of Potential Predictors of Hba1c Level in Diabetic Patients.

Variables	Regression Coefficient	Standard error	P value
Age(yr)	0.227	0.085	0.01
Sex(male/female)	-0.277-	0.609	0.651
Serum Mg	-0.963-	0.737	0.198
Duration of DM	-0.110-	0.134	0.416

Table 4 shows that HbA1c level is significantly correlated with serum magnesium level in diabetic patients while none of the age, sex and anthropometric data is significantly correlated.

Table 4: Correlations between serum magnesium level and some study parameters in diabetic patients.

Variable	Correlation coefficient	P value
Age(yr)	-0.165-	0.251
Sex	0.113	0.433
HbA1c %	-0.302-	0.033
Hb g/dl	0.001	0.996
MCV fl	-0.023-	0.875
WBCx 103/mm3	0.100	0.489
Neutrophil x 103/mm3	0.081	0.576
Lymphocyte x 103/mm3	0.053	0.715
Platelet count x 103/mm3	0.169	0.241

DISCUSSION

Of the most common diseases studied for their relation to serum Mg level is diabetes mellitus type 1. This is because of the significant role Magnesium plays a significant role in the metabolism of glucose and insulin, mainly through its direct effect on Glucose Transporter protein activity 4 and the regulation of glucose translocation into the cell^{10,11}.

In this study, we found that the mean serum magnesium level in patients with type 1 diabetes mellitus is lower than its level in controls and also the percentage of hypomagnesemia in the patients is significantly lower than its percentage in controls. This is in accordance with Asmaa et al¹² and Shahah et al¹¹ that found total serum magnesium was frequently low in Egyptian children with type 1 diabetes and it was correlated with HbA1c and also Ahmed et al,¹³ that found serum magnesium along with zinc and copper were lower in diabetics than controls. Likewise, Xu et al found that both serum and urine levels of magnesium were lower in Chinese diabetic patients¹⁴ and Lin et al found similar results in Chinese children⁷. Seyoumet al¹⁵ found a higher percentage of low serum magnesium (65%) in adults with both type I and type II diabetes by comparison to control which is even higher than our finding and Salmonowicz et al⁸ and Bjelakovic et al⁹ found also similar results. The coexistence of hypomagnesaemia with type 1 diabetes mellitus may be explained by osmotic diuresis that leads to magnesium loss. It is also thought that glycosuria in diabetics causes impairment of renal tubular reabsorption of magnesium and the deficiency of insulin is associated with increased urinary magnesium excretion¹⁶.

Inconsistent with our results, Matthiesen et al¹⁷ showed no statistically significant difference in serum magnesium level between Danish type I diabetic children and control group. Zargaret al¹⁸ found no significant difference in serum magnesium level between Indian type I diabetic children and control group and also Derakhshan et al in Iran¹⁹ and Ugurlu et al in Turkey²⁰ failed to find a significant difference. This difference may be related to differences among populations studied and the differences in glycemic control.

We observed in this study a negative correlation between serum magnesium level and HbA1c in diabetic patients. This is in agreement with Galli and Maggana¹⁰ that showed patients with poor glycemic control had a lower magnesium level. Moustafa et al¹² in Egypt, Alghobashy et al²¹ Arpacı in Turkey²² also found a similar negative correlation between serum magnesium level and diabetic control. This negative correlation can be explained by that uncontrolled hyperglycemia and hyperglycemia cause osmotic diuresis that may increase magnesium excretion¹².

Conversely, Lin *et al.*⁷ Salmonowicz et al,⁸ Matthiesen et al¹⁷ and Kundu et al²³ did not show any correlation between serum magnesium level and HbA1c in type 1 diabetic children and adolescents. This difference may be attributed to the difference in study populations, the good diabetic control and the different methods of serum magnesium and glycemic control evaluation.

We could not find any significant correlation between duration of diabetes and serum magnesium level in agreement with Lin *et al.*⁷ Salmonowicz et al,⁸ Moustafa et al¹² and Arpacı et al²² while

other studies found a significant negative correlation between the both like Shahbahet al,¹¹ Mishrahet al,²⁴ Ahmed and Helal,¹³ Alghobashy et al.²¹ This can be explained by different study populations and variable degree of diabetic control among these populations.

CONCLUSION

We concluded that serum magnesium level is frequently low in children with type 1 diabetes mellitus in Duhok and there is a significant correlation between serum magnesium level and the glycemic control. It is suggested to do regular monitoring of serum magnesium in type 1 diabetic children and to replace it if it is found low.

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ثوخته

ناستى ماڭنيسيومى لئاظ خوڭنى لدهف زاروكين توشبويين نيشا شەكرى جورى I .
ثەيوەندى لطل كوترولا شەكرى .

ئيشەكى: ماڭنيسيوم رولەكى طرنط يى ھەى ل مېتابولىزما كوربوھيدراتا دا كو رولە ھەى لستەر
ضېكرن و كاراكرنا انسولينى كو ئەو ھورمونه كوترولا ناستى شەكرا خوڭنى دكەت . ظەكولينا
سەرانسەرى جىھانە ديت كو ناستى ماڭنيسيومى لدهف زاروكين توشبوي شەكرى و كوترولا لاواز
يى نزمە .

ئارمانجا ظى ظەكولينى ھەلسەنطاندنا ناستى ماڭنيسيومى خوڭنى يە لدهف زاروكين توشبويين نيشا
شەكرى جورى I و ثەيوەندى وى لطل كوترولا شەكرى .

نەخوشان و ريك: ظەكولين ذ جورى كيس – كوترولا ھاتە كرن لستەر 50 توشبويين نيشا شەكرى
جورى I كو ذىي وان (1 تا 18) سال بو و ھەرۋەسا 50 كوتترول بېت طونجاي لطل وان ذ ئاليى
ذىي و رەطەزى . ناستى ماڭنيسيومى خوڭنى ھاتە ئىظان كو (1.7 ملغم/ دل) و تتر ھاتە ھىمارتن
ئاسايى . ناستى كوترولا لدويف ناستى (HbA1C) ھاتە دابەشكرن بو باش >7.5% ,
نەباش 7.5 – 8.5% , طەلەك نەباش < 8.5% .

داتا ھاتنە شروظەكرن بكارئىنانا (SPSS) فېرذن 22 . P كيمتر ذ 0.05 ھاتە ھىمارتن وەك طرنط .

نەنجام: ذ سەرجەم نەخوشان 32% ناستى ماڭنيسيومى يى كيم بو بقرورد لطل 10% ذ كوتترولان .
ناستى ماڭنيسيومى لدهف نەخوشان بقرنطىظە كيمتر بو ذ كوتترولان (P < 0.007) . ثەيوەندىكا
بقروظادى ياطرنط ھەبو دناظبەرا ماڭنيسيومى و كوترولا شەكرى (r=0.302 , P=0.03) .

سەرنەنجام: ناستى ماڭنيسيومى لئاظ خوڭنى يى نزمە لدهف زاروكين تو شبويين نيشا شەكرى جورى I .
ثەيوەندىكا طرنط ياهەى دناظبەرا ناستى ماڭنيسيومى و كوترولا شەكرى . ياطرنط ناستى
ماڭنيسيومى بھىتە ئىظان لدهف زاروكين توشبوي نيشا شەكرى و ماڭنيسيوم بھىتە دان بو ئەوين كيم
ماڭنيسيوم ھەى .

الخلاصة

حالة مغنسيوم الدم عند الاطفال المصابين بداء السكر النوع الاول و علاقتها بالسيطرة علي مستوى السكر

خلفية الدراسة و الهدف: يلعب المغنسيوم دوراً هاماً في أيض الكاربوهيدرات بحيث يؤثر على افراز و تنشيط الانسولين و هو الهرمون المنظم لمستوى السكر في الدم . مختلف الدراسات في شتى انحاء العالم اظهرت أن المصابين بداء السكر النوع الاول وسيطرة غير جيدة على مستوى السكر عندهم مستوى أقل من المغنسيوم في الدم . الهدف من هذه الدراسة هو قياس مستوى المغنسيوم في الدم عند الاطفال المصابين بداء السكرمن النوع الاول و دراسة علاقة ذلك بالسيطرة على مستوى السكر .

طريقة البحث: دراسة من نوع (حالة - مجموعة سيطرة) شملت 50 طفل مصاب بداء السكر من نوع الاول و 50 طفل متناسق معهم من حيث العمر و الجنس بدون داء السكر . تم قياس مستوى المغنسيوم عند الجميع و اعتبر المستوى 1.7 ملغم/ دل و اكثر هو الحد الطبيعي للمغنسيوم . السيطرة على السكر تم قياسها باستخدام (HbA1C) و صنف المرضى الى : جيد (أقل من 7.5 %) , غير جيد (7.5 - 8.5 %) و سيء جداً (اكثر من 8.5 %) . تم تحليل المعطيات احصائياً باستخدام (SPSS) الاصدار 22 و اعتبر $P < 0.05$ هامة احصائياً .

النتائج: وجد مستوى قليل من مغنسيوم الدم عند 32% من المرضى . مستوى المغنسيوم وجد أقل بشكل هام عند المرضى مقارنة بمجموعة السيطرة ($p < 0.007$) . وجدت علاقة عكسية هامة بين مستوى مغنسيوم الدم و مستوى السيطرة على السكر ($r = 0.033 = 0.302p$) .

الاستنتاج: مستوى مغنسيوم الدم قليل بشكل شائع عند الاطفال المصابين بداء السكر النوع الاول . توجد علاقة هامة احصائياً بين مغنسيوم الدم و مستوى السيطرة على السكر . توصي الدراسة باجراء مراقبة لمستوى المغنسيوم عند الاطفال المصابين بداء السكر النوع الاول وتعويض النقص بالمغنسيوم .