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 cut 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 1diabetic 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 glucose\(^1\). 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 sbone but it is not yet fully understood what regulators affect these organs at the cellular level\(^2\). Magnesium has a widespread role in 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 hormones. 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 ulcerations. Hypomagnesaemia also plays part in diabetic nephropathy. Hypomagnesaemia has been proposed to be a predictor of end-stage renal disease in diabetic nephropathy. Moreover; magnesium deficit leads to carbohydrate intolerance and insulin resistance and thereby induces or worsens diabetes mellitus.

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 controls. 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.

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.

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.
STATUS OF SERUM MAGNESIUM IN CHILDREN WITH TYPE 1 DIABETES

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 I. 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 al[12] and Shahah et al[11] 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 patients[14] and Lin et al found similar results in Chinese children[7]. Seyoumet al[15] 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 al[8] and Bjelakovic et al[9] 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 excretion[16].
Inconsistent with our results, Matthiesen et al\textsuperscript{17} showed no statistically significant difference in serum magnesium level between Danish type I diabetic children and control group. Zargar et al\textsuperscript{18} found no significant difference in serum magnesium level between Indian type I diabetic children and control group and also Derakhshan et al in Iran\textsuperscript{19} and Ugurlu et al in Turkey\textsuperscript{20} 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 Maggana\textsuperscript{10} that showed patients with poor glycemic control had a lower magnesium level. Moustafa et al\textsuperscript{12} in Egypt, Alghobashy et al\textsuperscript{21} Arpaci in Turkey\textsuperscript{22} 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 excretion\textsuperscript{12}. Conversely, Lin et al\textsuperscript{7}, Salmonowicz et al\textsuperscript{8}, Matthiesen et al\textsuperscript{17} and Kundu et al\textsuperscript{23} 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\textsuperscript{7}, Salmonowicz et al\textsuperscript{8}, Moustafa et al\textsuperscript{12} and Arpaci et al\textsuperscript{22} while other studies found a significant negative correlation between the both like Shahbahat et al\textsuperscript{11}, Mishrahet al\textsuperscript{24}, Ahmed and Helal\textsuperscript{13}, Alghobashy et al\textsuperscript{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 Duhokand 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.

REFERENCES

1. Rasheed H, Elahi S, Ajaz H. Serum magnesium and atherogenic lipid fractions in type II diabetic patients of Lahore, Pakistan. Biol Trace Elem Res. 2012; 148: 165–9. [PubMed]
2. Kaplinsky C, Alon US. Magnesium homeostasis and hypomagnesemia in children with malignancy. Pediatr Blood Cancer. 2013; 60: 734–40. [PubMed]
3. Lippincott Williams and Wilkins, Bishop ML, Fody EP, Schoef FL. Clinical Chemistry, Principles, Procedures and Correlations. 2005; 268–269; 327–330.
4. Pham PC, Pham PM, Pham SV, Miller JM, Pham PT. Hypomagnesemia in patients with type 2 diabetes. Clin J Am Soc Nephrol. 2007; 2: 366–373.
5. Sakaguchi Y, Shoji T, Hayashi T, Suzuki A, Shimizu M, et al. Hypomagnesemia in type 2 diabetic nephropathy: a novel predictor of end-

https://doi.org/10.31386/dmj.2019.12.1.7
6. Barbagallo M, Dominguez LJ. Magnesium metabolism in type 2 diabetes mellitus, metabolic syndrome and insulin resistance. Arch Biochem Biophys. 2007; 458: 40-47.
7. Lin CC, Tsweng GJ, Lee CF, Chen BH, HuangYL. Magnesium, zinc, chromium levels in children, adolescents, young adults with type 1 diabetes. Clin Nutr 2016; 35: 880–84. [PubMed]
8. 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: 259–68. [PubMed]
9. Bjelakovic G, Sokolovic D, Ljiljana S. Arginase activity and magnesium levels in the blood of children with diabetes mellitus. J Basic Clin Physiol Pharmacol. 2009; 20: 319–34. [PubMed]
10. Galli-Tsinopoulou A, Maggana I, Kyrgios I, Mouzaki K, Grammatikopoulou MG, Stylianou C et al. Association between magnesium concentration and HbA1c in children and adolescents with type 1 diabetes mellitus. J Diabetes. 2014; 6: 369–77. [PubMed]
11. Shahbah D, Abo El Naga A, Hassan T, Zakaria M, Beshir M, Al Morshedey S et al. Status of serum magnesium in Egyptian children with type 1 diabetes and its correlation to glycemic control and lipid profile. Medicine (Baltimore). 2016; 95(47): e5166
12. Asmaa MN, Samira SZ, Aliaa MM, Bassem HG. The Relationship between Hypomagnesaemia and Glycemic Control in Children with Type 1 Diabetes Mellitus. J Diabetes Metab. 2016; 7: 693.
13. Ahmed MM, Helal SR. A Study of Serum Magnesium, Zinc, Copper and Glycohemoglobin In Children with Type 1 Diabetes Mellitus. Alexandria Journal of Pediatrics. 2002; 16(2): 285-9.
14. Xu J, Xu W, Yao H, Sun W, Zhou Q, Cai L. Associations of Serum and Urinary Magnesium with the Pre-Diabetes, Diabetes and Diabetic Complications in the Chinese Northeast Population. 2013; 8(2): 56750.
15. Seyoum B, Siraj ES, Saenz C, Abdulkadir J. Hypomagnesemia in Ethiopians with diabetes mellitus. Ethn Dis. 2008; 18: 147–51. [PubMed]
16. Farid SM, Abulfaraj TG Trace mineral status related to levels of glycated haemoglobin of diabetic subjects in Jeddah, Saudi Arabia. Medical Journal of Islamic World Academy of Sciences. 2013; 21: 47-56.
17. Matthiesen G, Olofsson K, Rudnicki M. Ionized magnesium in Danish children with type 1 diabetes. Diabetes Care. 2004; 27: 1216–7. [PubMed]
18. Zargar AH, Bashir MI, Masoodi SR, Wani BA, Wani AI, Khan AR et al. Copper, zinc and magnesium levels in type-1 diabetes mellitus. Saudi Med J. 2002; 23(5): 539-542.
19. Derakhshan R More Derakhshan R, Balaee P, Darakhshan S, Masoodpoor N, Banihosseini SS. Lipid profile, thyroid function, and serum magnesium level in type I diabetic children Minerva Pediatrica. 2011; 63(1): 27-33.
20. Uğurlu V, Binay C, Şimşek E, Bal C. Cellular Trace Element Changes in Type 1 Diabetes Patients. J Clin Res Pediatr Endocrinol. 2016; 8(2):180–6.

21. Alghobashy AA, Alkholy UM, Talat MA, Abdalmonem N, Zaki A, Ahmed IA et al. Trace elements and oxidative stress in children with type 1 diabetes mellitus. Diabetes Metab Syndr Obes. 2018;11:85–92.

22. Arpaci D, Tocoglu AG, Ergenc H, Korkmaz S, Tamer A. Associations of serum Magnesium levels with diabetes mellitus and diabetic complications. Hippokratia. 2015;19(2):153–7.

23. Kundu D, Osta M, Mandal T, Bandyopadhyay U, Ray D, Gautam D. Serum magnesium levels in patients with diabetic retinopathy. J Nat Sci Biol Med. 2013;4: 113-6.

24. Mishra S, Padmanaban P, Deepthi GN, Sarkar G, Sumathi S, Toora BD.. Serum magnesium, dyslipidemia in type-2 diabetes mellitus. Biomed Res. 2012;23:295–300.
STATUS OF SERUM MAGNESIUM IN CHILDREN WITH TYPE 1 DIABETES

ثوختة

نستى ماطنيسيومي لناظ خوينى لدقف زاروکین توشبوین نیشا شاکری جوری I

ثاتیوتدی لاطال کونترولوا شاکری.

ئیشى: ماطنيسيوم روول акی طرنت بي هه تا ل میتاژزویا كوربوهیدراتا دا کو روولو هه لستر ضیکرنا. و کاراکرنا انسلینی کو نگه هورمونة کونترولوا نستى شاکرنا خوینی دکات . ظاکونیا سترانسیتشی جیهانی دیت کو نستى ماطنيسيومي لدقف زاروکین توشبوی شاکری و کونترولا لازم.

نارمینجا گی ظاکونیا هیژنسیتاندا ناستي ماطنيسيومي خویني ية لدقف زاروکین توشبوین نیشا شاکری جوری I و ثاتیوتدیا ىی لاطال کونترولوا شاکری.

تخوشان و ریک: ظاکونیا ز جوری کیش - کونترولة هاتة كرن ىسارت 50 توشبوین نیشا شاکری جوری I کو نگه وان (1 تا 18) سال بو و هترومسا 50 کونترول بیت ئجوج ىی لاطال وان ذ نالی ىی ذبی و رختی ت. ناستى ماطنيسيومي خوینی هاتة ثیطان کو (1.7 ملغم/دل) و تطر هاتة هنمارتن ناسایى. ناستى کونترولا لدویف نستى (HbA1C) هاتة دایشکرنا بو باش.7–5%.

نةخؤشان و ریک: ناتسي کونترولا لدقف نستى (HbA1C) هاتة دایشکرنا 0.50 هاتة هنمارتن هیپ طرنت.

نةنجم: ذ سترجعتم ناخوشان 32% ناتسي ماطنيسيومي بي كيم بو بتراود لاطال ىی 10% ذ کونترولوان. ناتسي ماطنيسيومي لدقف ناخوشان بطرطیطة کیمت بو ذ کونترولوان (P<0.007). ثثیوتدیا باطرطیدا بطتر هاتو دناظیتا ماطنيسيومي و کونترولا شاکری (r=0.302, P=0.03).

سسترنهنجم: ناتسي ماطنيسيومي لناظ خویني ية لدخف زاروکین تو شبیین نیشا شاکری جوری I.

ثثیوتدیا بطیره دناظیتا ناتسي ماطنيسيومي و کونترولا شاکری. بطیره ناتسي ماطنيسيومی بهیتة ثیطان لدخف زاروکین توشبی نیشا شاکری و ماطنيسيوم بهیتة دان بو ناوین کیم ماطنيسيومی هاى.
الخلاصة

حالة مغنيسيوم الدم عند الأطفال المصابين بداء السكر النوع الأول و علاقتها بالسيطرة على مستوى السكر

خلفية الدراسة:
يلعب المغنيسيوم دوراً هاماً في أيض الكاربوهيدرات بحيث يؤثر على إفراز و تنشيط الأنسولين و هو الهرمون المنظم لمستوى السكر في الدم . مختلف الدراسات في شتى أنحاء العالم أظهرت أن المصابين بداء السكر النوع الأول وسيطرة غير جيدة على مستوى السكر عندهم مستوى أقل من المغنيسيوم في الدم . الهدف من هذه الدراسة هو قياس مستوى المغنيسيوم في الدم عند الأطفال المصابين بداء السكر من النوع الأول و دراسة علاقة ذلك بالسيطرة على مستوى السكر.

طريقة البحث: دراسة من نوع (حالة - مجموعة سيطرة) شملت 50 طفل مصاب بداء السكر من نوع الأول و 50 طفل متناسق معهم من حيث العمر و الجنس بدون داء السكر. تم قياس مستوى المغنيسيوم عند الجميع و أعتبر المستوى 1.7 ملغم/ دل و أكثر هو الحد الطبيعي للمغنيسيوم . السيطرة على السكر تم قياسها باستخدام (HbA1c) و صنف المرضى إلى: جيد (أقل من 7.5% )، غير جيد (7.5 – 8.5%) و سيء جداً (أكثر من 8.5%) . تم تحليل المعطيات إحصائياً باستخدام SPSS (الإصدار 22 و اعتبار 0.05 هامة إحصائياً).

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

الاستنتاج: مستوى مغنيسيوم الدم قليل بشكل شائع عند الأطفال المصابين بداء السكر النوع الأول . وجدت علاقة هامة إحصائياً بين مغنيسيوم الدم و مستوى السيطرة على السكر . توصي الدراسة بإجراء مراجعة لمستوى المغنيسيوم عند الأطفال المصابين بداء السكر النوع الأول وتعويض النقص بالمغنيسيوم.