

Evaluation of the Influence of Diabetic Control on Vitamin B12 Levels in Children and Adolescents with Type 1 Diabetes

Yasmin G. Mohamed¹, Noha M. Kamel², Sara A. Hennawi^{3*}, Amina M. Abdel Wahab¹, Enas F. El Nagar¹

¹Department of Pediatrics, Faculty of Medicine, Suez Canal University, Egypt.

²Department of Clinical Pathology, Faculty of Medicine, Suez Canal University, Egypt.

³Department of Pediatrics, Faculty of Medicine, Port Said University, Egypt.

Abstract

Aim: The study aims to evaluate the influence of diabetic control on vitamin B12 levels. **Patients and Methods:** The study was conducted on 40 children diagnosed with type 1 Diabetes Mellitus, who attended El Arab school health insurance unit in Port-Said City. Serum vitamin B12 and diabetic profile (fasting, random blood sugar, and HbA1c) were sampled and values below the limit of the blank are reported as < 50.0 pg/mL or < 36.9 pmol/L and values above the measuring range are reported as > 2000 pg/mL or > 1476 pmol/L. HbA1c measurement was used for the assessment of diabetic control. **Results:** The average age of patients was 9 years. The mean FPG was 142 mg/dL, the mean RBS was 221 mg/dL, and the mean HbA1c was 10.13%. The mean duration of diabetes was 4±2 years. All studied patients showed normal vitamin B12 levels. The mean serum vitamin B12 level was 687pg/m and there was no statistically significant correlation between B12 and HbA1c. **Conclusion:** The mean HbA1c among type 1 diabetic patients who attended El Arab School health insurance unit in Port-Said City was 10.13%. There is no relation between serum vitamin B12 level and duration of diabetes or diabetic control.

Keywords: children, DM

Introduction

Diabetes is a group of metabolic diseases characterized by hyperglycemia resulting from deficiency in insulin secretion, poor insulin action, or both⁽¹⁾. Type 1 diabetes mellitus (T1DM) (Insulin Dependent Diabetes Mellitus: IDDM) results from the autoimmune destruction of insulin-producing beta cells and is characterized by the presence of insulinitis and beta-cell autoantibodies. It is also associated with other

autoimmune endocrine disorders that developed from the harmful effect of the autoantibodies leading to autoimmune polyglandular syndrome⁽²⁾. Vitamin B12 or cobalamin is a water-soluble vitamin that has a main role in DNA synthesis, erythropoiesis, and nerve function. Therefore clinical features of vitamin B12 deficiency are predominantly those of haematological and neurocognitive dysfunction⁽³⁾. Vitamin B12 deficiency causes permanent debilitating peripheral neuropathy, balance and gait

*Corresponding Author: saraamr@med.suez.edu.eg

disorders, tremors, frequent falls, and visual disturbances. Chronic vitamin B12 deficiency can result in demyelination of the nerves and spinal cord which may lead to partial or complete paralysis. Vitamin B12 deficiency can be manifested with the same complication of diabetic neuropathy as autonomic neuropathy as (i.e. gastroparesis, impotence, urinary incontinence). It can also result in optic neuropathy and optic nerve atrophy, as well as retinal disease⁽⁴⁾. Biochemical and clinical vitamin B12 deficiency has been demonstrated to be prevalent among patients with type 1 and type 2 diabetes mellitus (T2DM)⁽⁵⁾. However, there is insufficient data regarding the association between vitamin B12 deficiency and T1DM in the Egyptian population. Hence this study was undertaken to evaluate serum B12 levels in type 1 diabetic patients and its relation to diabetic control in the Egyptian population attending a primary care unit, to assess the need for regular screening and supplementation of vitamin B12.

Subjects and Methods

Patient Selection

The study group consisted of type 1 diabetic patients attending El Arab school health insurance unit in Port-Said City. Forty patients with T1DM were enrolled in this study, and they were aged less than 18 years and were from both sexes. Exclusion Criteria were patients who are strict vegetarians, patients with a history of malabsorption syndromes, previous gastrectomy, and patients on drugs known to interfere with vitamin B12 absorption, such as phenytoin, dihydrofolate reductase inhibitors, proton pump inhibitors, and metformin. All patients were subjected to adequate history taking through interviews with one or both parents including personal data, diabetes history including

onset of diagnosis, regimen of treatment and complications if present, past medical history including any chronic illness or operations, drug history as certain medications may contribute to vitamin B12 deficiency as proton pump inhibitors⁽⁶⁾ and metformin⁽⁷⁾. Nutritional history excludes vegetarians. present history as symptoms of vitamin B12 deficiency as weakness, tiredness, lightheadedness, palpitations, shortness of breath, pallor, anorexia, neurological problems like numbness or tingling, muscle weakness, and mental problems like depression, memory loss, or behavioral changes. Clinical examination of all systems was done including neurological examination for neuropathy, signs of vitamin B12 deficiency as glossitis, progressive weakness, ataxia, and paresthesias that may progress to spasticity and paraplegia, and signs of uncontrolled hyperglycemia as candidal infection. Laboratory investigations were done. Serum Vitamin B12 level was estimated by a fully automated electrochemiluminescence (ECLIA) immunoassay analyzer; Cobas e411 (Roche Diagnostics, Germany). Diabetic profile (Fasting, random blood sugar, and HbA1c), was performed by Cobas c 501 (Roche Diagnostics, Germany) and APCA was estimated by ELISA, for exclusion of PA.

Specimen collection and storage

A five-ml sample was collected by venipuncture, and whole blood was divided into two tubes: an EDTA-containing tube for HbA1c and a plain tube for the other laboratory tests. Blood was allowed to clot, and serum was separated by centrifugation at 3000 rpm for 10 minutes and stored at 20°C.

Operational definitions

T1DM was diagnosed based on history, clinical evaluation, and laboratory findings. According to the American Diabetes Association criteria⁽⁸⁾ as follows FPG level ≥ 126

mg/dL (7.0 mmol/L), or a 2-hour PPG ≥ 200 mg/dL (11.1 mmol/L) during a 75-g OGTT, or a random plasma glucose ≥ 200 mg/dL (11.1 mmol/L) in a patient with classic symptoms of hyperglycemia or hyperglycemic crisis, or HbA1C measurement: ≥ 6.5 percent. Vitamin B12 levels were considered deficient with a value less than 148 pmol/L (200 pg/mL)⁽⁹⁾.

Statistical Analysis

Data was collected then tabulated and analyzed using computer facilities. Statistical analysis was performed using standard methods using Statistical Package of Social Science (SPSS) version 17. Count, percent, Mean, and standard deviation were estimated for each continuous variable. A chi-square test and an independent t-test were used to assess the statistical difference between variables, and each test was

administered according to the variable type. Statistical significance was considered at P-value < 0.05 . Study results were described in tables and graphs.

Results

The study included 40 diabetic patients, 16 of which were males and 24 were females. The average age of patients was 9 years (Table 1). The mean duration of diabetes in patients in this study was 4 ± 2 years (Table 2). There were non-statistically significant correlations between serum vitamin B12 and HbA1c, FBS, and RBS (Table 3). There was a non-statistically significant correlation between vitamin B12 and age among the studied participants (Table 4). There was a non-statistically significant correlation between vitamin B12 and hemoglobin level (Table 5).

Table 1: characteristics of the participants (n=80).		
Characteristics		(n=40)
Age (years)	Mean \pm SD	9 \pm 3
	Median (min-max)	9(2.3-16)
Gender	Male	16(40)
	Female	24(60)

Table 2: Duration of DM of the studied patients (n=40).		
Duration of DM (years)	Mean \pm SD	4 \pm 2
	Median (min-max)	3.6(0.4-11)

Table 3: Correlations between vitamin B12 and HbA1c, FBS and RBS among the participants (n=80).				
Correlations		HbA1c	FBS	RBS
Vitamin B12	Pearson Correlation	-0.194	-0.152	-0.005
	P-value	0.231	0.348	0.974
	N	40	40	40

Discussion

Type 1 diabetes mellitus (T1DM) is a metabolic disease that results from the autoimmune destruction of insulin-producing beta cells and is characterized by the presence of insulinitis and beta-cell autoantibodies⁽²⁾. Vitamin B12 or cobalamin is a water-soluble vitamin that has a fundamental role in DNA synthesis, erythropoiesis, and nerve function⁽³⁾. Vitamin B12 deficiency due to pernicious anemia (PA) occurs frequently among patients with T1DM⁽¹⁰⁾. In

addition, dietary habits that vary from one person to another could also contribute to the deficiency⁽¹¹⁾. Unfortunately, the symptoms of diabetic neuropathy overlap with paresthesia, impaired vibration sense, and impaired proprioception associated with vitamin B₁₂ deficiency. Therefore vitamin B₁₂ deficiency-induced nerve damage may be confused with or contribute to diabetic peripheral neuropathy⁽¹²⁾. Worsening diabetic neuropathy is also noted among patients with co-existing vitamin B12 deficiency⁽¹³⁾.

Table 4: Correlation between vitamin B12 and age among the participants (n=80).		
Correlations		Age
Vitamin B12	Pearson Correlation	-0.178
	P-value	0.271
	N	40
	P-value	0.253
	N	40

Table 5: Correlation between vitamin B12 and hemoglobin among participants (n=80).			
Correlation			Hb
Case	Vitamin B12	Pearson Correlation	-0.083
		P-value	0.61
		N	40
		P-value	0.356
		N	40

Because of the previously mentioned cause, identifying the correct etiology of neuropathy is crucial, because simple vitamin B12 replacement may reverse neurologic symptoms inappropriately attributed to hyperglycemia⁽¹⁰⁾. On the other hand, excess of vitamin B6 (pyridoxine) -which is present in most vitamin B complex preparations is harmful; sensorimotor neuropathy secondary to pyridoxine toxicity can be debilitating⁽¹⁴⁾. Vitamin B6 toxicity produces sensory ataxia, areflexia, and

impaired cutaneous sensation. Patients often complain of burning or paresthesias. Electrodiagnostic testing usually shows a sensory neuronopathy, but with severe toxicity motor nerves can be affected as well. Symptoms of toxicity can be seen with doses as low as 100 mg per day⁽¹⁵⁾. There is insufficient data regarding the association between vitamin B12 deficiency and T1DM in the Egyptian population. Also, it is noticed that vitamin B12 supplementation (mostly as vitamin B complex

preparations) was given routinely for all type 1 diabetic children, in most health insurance care units without screening. Hence, this study was performed to evaluate serum B12 levels in type 1 diabetics in Egyptian population attending a health insurance care unit, to assess the need for regular screening and supplementation of vitamin B12 in type 1 diabetics. In this study the average age of patients was 9 yrs, so presence of old age is as a risk factor for vitamin B12 deficiency in our study is excluded, as in general, vitamin B12 level declines with age and prevalence of vitamin B12 deficiency increases with age⁽¹⁶⁾. Also patients were tested first for APCA (antiparietal cell antibody), three patients were positive and were excluded, and those who tested negative were included. APCA was chosen for exclusion of PA (pernicious anemia) as they are present in most cases, about 85-90%^(17,18), and therefore it is an adventitious tool for screening of PA⁽¹⁹⁾. The mean FPG was 142 mg/dL, while the RBS was 221 mg/dL and the mean HbA1c was 10.13%. In our study, all patients of the study group showed normal vitamin B12 levels. The mean serum vitamin B12 level was 687 pg/ml. Only one patient had a borderline vitamin B12 level (222 pg/ml). In another study done in a tertiary care hospital in India on 90 T1DM patients whose ages ranged from 3 to 28 years, the prevalence of low serum vitamin B12 was found to be 45.5%. Out of this, 28.5% had values in the deficient range while 17% were in the indeterminate range⁽¹⁰⁾. These contrary results may be attributed to differences in both population groups, although the age of the studied population was comparable, their study sample consisted of patients from various regions of Karnataka registered with the Bangalore Diabetes Registry, who followed different dietary habits, and a detailed dietary history was not available⁽¹⁰⁾, so B12 deficiency may be due to nutritional

deficiencies while in our study adequate intake of vitamin B12 from dietary sources was ensured. Also, the presence of APCA was not assessed in the other study, so its role can't be excluded, while in our study cases with positive APCA were excluded from the study. Our results were matching with that of a case control study done in Italy which was done on T1DM patients with mean age of 16.7 yrs., and mean diabetes duration of 8.4 yrs., where serum vitamin B12 levels were normal in all patients, with mean levels of 698 pg/ml in females and 832 pg/ml in males⁽²⁰⁾. The mean duration of diabetes in the studied group in our study was 4 yrs, ranging from 0.4 to 11 years duration. There was a non-statistically significant correlation between vitamin B12 levels and duration of diabetes in the studied group. This is similar to what was found in another study in India where no correlation between vitamin B12 and the duration of diabetes was found⁽¹⁰⁾. Moreover, in our study, there were no statistically significant correlations between vitamin B12 and other variables; age, HbA1c, FBS, RBS and Hb level among the studied participants. This was in agreement with the other study in India as there was also no correlation between vitamin B12 and diabetes control (HbA1c) or age⁽¹⁰⁾. In another case control study done in Italy, on 41 patients (21 males and 20 females) with T1DM, all were Caucasians, vitamin B12 levels were significantly higher only in male patients than in male controls⁽²⁰⁾. This difference may be related to different ethnic groups of the studied population or nutritional habits.

Conclusion

The mean HbA1c among type 1 diabetic patients who attended El Arab school health insurance unit in Port-Said city was 10.13% with an average duration of diabetes about

4 years duration. There is no correlation between serum vitamin B 12 level and duration of diabetes or diabetic control (HbA1c) or age of the patients. So, the neuropathy symptoms that manifested in type 1 diabetic children could be related to the diabetic neuropathy more than the vitamin B12 deficiency.

Limitations of the study

Other markers for vitamin B12 deficiency such as MMA (methylmalonic acidemia) test and holoTC (holotranscobalamin) test were not evaluated, due to high cost. Elevated MMA and Hcy (homocysteine test) levels improve the diagnosis of tissue B12 deficiency, especially in cases with borderline B12 levels⁽²¹⁾.

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