

Vitamin B12 deficiency in turkish patients with Type 2 Diabetes Mellitus

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ABSTRACT

Objective: Type 2 diabetes (T2DM) disease and related changes in blood parameters bring essential health risks. This study was carried out to determine the frequency of vitamin B12 deficiency in T2DM patients, the effect of B12 deficiency on blood glucose, HbA1c control and lipid parameters, and the B12 level in diabetes patients using metformin.

Material and Methods: 287 patients with T2DM who were followed up in the Endocrinology department of Istanbul Training and Research Hospital were evaluated. After the patients called for control had fasted for 8 hours, blood tests were performed, and biochemical parameters were determined with standard laboratory techniques. Vitamin B12 <180 mg/dl was accepted as a deficiency, and patients were divided into groups regarding vitamin B12 deficiency. The chemiluminescence method was used to determine serum Vitamin B12 levels. Data were analyzed using SPSS version 22.0 (IBM Corporation, Armonk, NY, USA).

Results: A total of 287 T2DM patients were included in the study. B12 deficiency is present in 29.8% of T2DM patients. Vitamin B12 values were found to be lower in patients with T2DM using metformin (280.2 pg /ml ±151.06 pg/ml, p<0.05); however, lower vitamin B12 values did not have a significant effect on blood sugar control (p=0,3), and hypovitaminosis Vitamin B12 was associated with elevated hypertriglyceridemia (p=0,03).

Conclusion: According to the current study, serum vitamin B12 level was not associated with blood glucose and HbA1c; a relationship was found between vitamin B12 deficiency and higher hypertriglyceridemia. A significant proportion of T2DM patients using metformin had lower levels of vitamin B12 compared to T2DM patients not using metformin. Vitamin B12 levels should be monitored regularly in the follow-up of patients with T2DM using metformin.

Keywords: Type 2 Diabetes mellitus; Metformin; Vitamin B12 deficiency

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INTRODUCTION

Type 2 Diabetes Mellitus encumbers a significant population health problem worldwide, and Turkey has classical and modern direct and adjunctive treatment options in health practice (1). While many options are added continuously every day in terms of treatment, adjunctive treatment options are also sometimes clinical practice.

These personalized treatment options include pre-probiotics, and replacement of deficient vitamins and minerals (2,3). Vitamin B12, one of these vitamins, has attracted clinical significance, while its deficiency could be practised with some treatment models (4).

In this study, we aimed to investigate Vitamin B12 deficiency and its effect on blood glucose control and lipid parameters in Turkish patients with Diabetes Mellitus.

MATERIAL and METHODS

In a cross-sectional study of 312, previously diagnosed consecutive Type 2 DM patients (according to American Diabetes Association criteria (5)) who were routinely followed by Istanbul Research and Education Hospital Endocrinology department were included. Patients with malabsorption, cardiovascular or cerebrovascular disease, malignant cancer, pregnancy, any medication affecting Vitamin B12 levels (proton pump inhibitor, multivitamins), alcoholism, or active infection were excluded from the study. After exclusion criteria, a total of 287 patients with T2DM were enrolled. Blood was collected after an overnight fast, and biochemical parameters were determined with standard laboratory techniques. The patients were divided into groups in terms of HbA1c level (<7 %, =7-10 %, >10) and Vitamin B12 deficiency. The HbA1c groups were compared in terms of mean Vitamin B12 and Vitamin B12 deficiency. Vitamin B12 < 180 pg/ml was accepted as a deficiency (6). The chemiluminescence method was used to determine serum Vitamine B12 levels ((Beckman Coulter UniCel D×1 600).

The study was carried out according to the Declaration of Helsinki, and the protocol was approved by the Ethics Committee of Istanbul Research and Education Hospital (23.12.2022/405). Informed consent was taken from all patients.

The chi-square test was used for categorical data; the Student's t-test and ANOVA test were used for group comparisons. The normal distribution was evaluated with Shapiro-Wilk's test.

The variables with normal distribution were presented as mean ± standard deviation (SD), and those not in normal distribution were presented as median. P<0.05 within a confidence interval of 95% was considered statistically significant.

Data were analyzed using SPSS version 22.0 (IBM Corporation, Armonk, NY, USA.)

RESULTS

Two hundred eighty-seven patients with a mean age of 56,08 (min:26-max:86) have been enrolled. 51,9 (n=49) % of the patients were female, and the median diabetes duration was ten years. Vitamin B12 deficiency was found in 29.8 % (85/87) of the patients. The descriptive characteristics of the study group are shown in Table 1.

The analysis of metabolic parameters of the patients in the vitamin B12-deficient (group 0) and vitamin B12-sufficient groups (group 1) are shown in Table 2. The mean triglyceride number in the vitamin B12-deficient group (group 0) (61.36, sd=245.47, N=86) was different from the mean triglyceride number in the vitamin B12-sufficient group (group 1) (195.49, sd=122.12). p=0,03) (Table 2)

The mean serum B12 level in the metformin medication group was found to be significantly lower. 280.1±151.0 vs 356.02±195.21 pg/ml (p<0.01, Table3)

No significant difference was found according to HbA1c levels. Mean Vitamin B12 levels were insignificantly lower in higher HbA1c levels (p=0.58, Table 4)

Table 1: Characteristics and Blood Values of the Study Population

	N	Minimum	Maximum	Mean/Median	Std. Deviation
Age (years)	287	26	80	56	N/A
Height (cm)	286	143,00	195,00	162,9231	10,14462
Body Mass Index (kg/m ²)	286	20,96	64,49	34,1029	6,86841
Diabetes Duration (years)	268	1	40,0	10	N/A
Vitamin B12 (pg/ml)	287	90	849	257.5	157.36
HbA1c (%)	285	5,6	14,8	9,01	1.86
Glucose (mg/dl)	287	77	355	186	62.27

Table 2: Metabolic Values According To Vitamin B12 Deficiency

Parameter	B12 Levels	N	Mean	Std. Deviation	P Value
Glucose (mg/dl)	0	86	196,7442	73,06664	0,30
	1	201	207,5323	85,46099	
Hba1c (%)	0	86	8,7907	2,27506	0,66
	1	199	8,9095	2,06154	
LDL (mg/dl)	0	78	135,7821	44,67419	0.29
	1	192	128,9531	49,35174	
HDL-c (mg/dl)	0	85	45,3563	34,61616	0,33
	1	200	49,5792	33,55601	
Tryglyceride (mg/dl)	0	85	261,3605	245,46925	0,03
	1	200	195,4851	122,12359	

0: Vitamin B12 deficient group, 1: Vitamin B12 sufficient group, p value<0.05= significant, student't t test for groups comprasion

Table 3: Mean Vitamin B12 levels according to metformine usage

Metformine usage	N	Mean Vitamin B12 (pg/ml)	Std. Deviation	P
0	85	356,8298	195,21408	P<0.01
1	202	280,1719	151,06369	

0: Not using metformin, 1: Using metformin. value<0.05

Table 4: Vitamin B12 Levels According To HbA1c Groups

Groups	Vitamin B12(pg/ml)	P Value A/B	P Value B/C	P Value A/C	P Value A/B/C
A: HbA1c <7 % (n=24)	282.33±132.97	0.72	N/A	0.34	0.58
B: HbA1c 7-10% (n=189)	295.11±197.21	0.72	0.38	N/A	
C: HbA1c >10% (n=72)	315.26±166.04	N/A	0.38	0.34	

DISCUSSION

The current study has shown that vitamin B12 deficiency was 29.8 % in our study population. This ratio was consistent with other national studies, as 32.4% in Oman (7) and 28.3% in Malaysia. (8) T2DM patients on metformin medication had lower Vitamin B12 values (280.2 pg /ml ±151.06 pg/ml, p<0.05); however, lower Vitamin B12 values didn't produce any significant effect on blood glucose control but were associated with higher hypertriglyceridemia.

Vitamin B12 levels should be worked out in the suspicion of megaloblastic anemia or neurologic symptoms according to guidelines (9); however, metformin treatment has been found to be associated with Vitamin B12 deficiency (10). The duration of this treatment and the metformin dose was found to be the best indicators of vitamin B12 deficiency development (11). Moreover, it has been speculated that even with coincident vitamin B12 deficiency, metformin usage did not bring our typical Vitamin B12 deficiency symptoms, likewise anemia or neuropathy, after 4.9 years of treatment (12). However, another study from India found an increased risk for peripheral neuropathy after metformin treatment. (13) In a review of Vitamin B12 supplementation and peripheral neuropathy, 2 of 5 studies showed significant improvement in peripheral neuropathy (14) The reason for vitamin B12 deficiency with metformin treatment is the inhibition of vitamin B12-IF complex in the terminal ileum (15).

The current study found higher hypertriglyceridemia with Vitamin B12 deficiency. Contrary to our study, a study from Poland with 62 patients didn't find any association between B vitamins and hyperlipidemia (16). The current concept that drives us to investigate this association is malonyl-CoA accumulation due to vitamin B12 deficiency, which could result in increased lipogenesis and inhibit fatty acid oxidation (17).

According to this study, serum vitamin B12 level was found not to be associated with blood glucose and HbA1c. A recent study has found that vitamin B12 replacement could improve glycemic control and blood glucose fluctuations (18). However, another study demonstrated that hyperglycemia alters vitamin B12 usage in the body and thus increases serum B12 levels (19).

When we classified our study group according to HbA1c, we could not find significantly higher vitamin B12 levels. Higher vitamin B12 levels were associated with a decline in 24 h melatonin levels and sleep quality. Moreover, the increased incidence of insomnia seemed to increase with using mecobalamine (20). Therefore the balance with the replacement of vitamin B12 should be done meticulously. It is difficult to estimate whether sleep problems due to high vitamin B12 levels could cause higher HbA1c and worsened blood glucose control.

Limitations of our study are its cross-sectional design, one center study. However, the number of patients was considerably high and represented a high spectrum of patients from Turkey due to its central location.

CONCLUSION

Vitamin B12 deficiency is common in patients with T2DM. Patients who use metformin as medication showed a higher frequency of vitamin B12 deficiency. Vitamin B12 deficiency was associated with higher triglyceride but not glucose levels in Turkish patients with T2DM.

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Author Contributions İGK, SK, and BH; Study design, Data collection, and analysis. **İGK, SK;** Writing, literature review, and revisions. **İGK;** Submission of the manuscript.

Ethical approval: All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and/or with the Helsinki Declaration of 1964 and later versions. This study was conducted with the approval of the local ethics committee of the University of Health Sciences, Istanbul Training, And Research Hospital (decision date 23.12.2022 and numbered 405).

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