

B12 Deficiency: An Unexpected Cause of Urinary Incontinence

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ABSTRACT

Urinary incontinence (UI) is a common and important health problem in society. It has negative effects on individuals' daily life activities and quality of life.

Our study aims to assess the relationship between vitamin B12 and urinary incontinence.

109 patients (80 women, 29 men) diagnosed with urinary incontinence at Recep Tayyip Erdogan University between January 2018 and December 2023 were retrospectively examined. As a control group, 100 healthy individuals (66 females, 34 males) of similar age to the patients were included. Vitamin B12 levels were measured using the Electrochemiluminescence Immunoassay (ECLIA) method. UI was assessed with specific questions regarding stress and urge incontinence.

There was no difference in age when we compared the control and patient groups (44.76 and 43.6 years, respectively).

Vitamin B12 levels were lower in the patient group compared to the control group ($p=0.001$). When we compared the folate levels in the patient group, they were lower than in the control group ($p=0.035$).

In our study, we found a significant association between vitamin B12 deficiency and urinary incontinence. B12 deficiency contributes to pelvic floor dysfunction through neurological and structural changes. These results suggest that treatment of vitamin B12 deficiency may play an important role in the management of urinary incontinence.

Keywords: Urinary Incontinence, Vitamin B12 deficiency

Introduction

Vitamin B12 is a water-dissolvable vitamin that plays crucial biological roles in the body. Its primary role is its necessity for cell division and DNA synthesis. Vitamin B12 is absorbed in the terminal part of the small intestine by binding to intrinsic factor (IF), which is produced by the stomach's parietal cells (1). Most of the B12 in the body is stored in the liver, and this storage is at a level that will meet the body's needs for about three years. Vitamin B12 is mostly obtained from animal foods, and B12 deficiency is rarely seen in individuals who consume sufficient amounts of animal products and do not have digestive system diseases (2).

Urinary incontinence (UI) is a common health trouble that can be seen at a rate of 12-49.9% with different severities. The most prevalent form of

UI is stress urinary incontinence (SUI) (3,4). SUI occurs when intra-abdominal tension increases, such as during intense physical activities, coughing or sneezing, when urethral pressure exceeds maximum levels. Urinary incontinence can negatively affect the quality of life by limiting the participation of individuals in daily life activities. In addition, this condition can increase the risk of depression, reduce participation in social and physical activities, negatively affect sexual health, and increase the frequency of perineal dermatitis and infection (5-7). Common causes of urinary incontinence include dysfunction of the pelvic muscles, weakness in the pubourethral ligaments, and birth-related trauma (3,4).

Pelvic structures are rich in collagen, and collagen is a protein composed of proteoglycans derived from amino acids. The role of collagen in the periurethral support structure is extremely

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Received: 01.01.2025, Accepted: 18.08.2025

important. B12 vitamin deficiency can lead to disruptions in collagen synthesis, which can lead to dysfunction of pelvic structures and, as a result, to the development of urinary incontinence. However, research exploring the connection between vitamin B12 levels and UI is limited (8).

Our study aims to assess the relationship between vitamin B12 and urinary incontinence

Materials and Methods

This retrospective study was conducted on a total of 109 patients (80 female, 29 male) diagnosed with urinary incontinence at Recep Tayyip Erdoğan University between January 2018 and December 2023. As the control group, 100 healthy individuals (66 female, 34 male) who were age-matched to the patient group and did not have urinary incontinence were selected. A medium effect size ($d = 0.50$) was obtained for the independent two-sample t-test with 100 cases in the control group and 109 cases in the patient group, assuming 95% power and a 5% margin of error (9). The power analysis indicated that the designated sample size would facilitate the establishment of reliable inferences within the study (10). Power analysis was evaluated with the GPower 3.1 program (11). The study was conducted according to the Declaration of Helsinki. Ethical approval no: 2023/23.

Exclusion Criteria: The study excluded individuals with diabetes, a history of cerebrovascular accidents, advanced pelvic organ prolapse (POP), or those who required surgical treatment. Additionally, participants who were vegetarians, used estrogen replacement therapy, took vitamins, analgesics, proton pump inhibitors (PPIs), or H2 receptor blockers, or were on diuretics and medications for urinary incontinence were also excluded. Other exclusions included patients with cancer, thyroid disorders, metabolic conditions, pernicious anemia, osteoporosis, celiac disease, Crohn's disease, Whipple's disease, or gastrointestinal issues such as those who had undergone gastric surgery. Furthermore, individuals who chose not to participate in the study were excluded.

Data Gathering: The participants' age, sex, body mass index (BMI), clinical condition, medications, surgical history, existing health issues, and urological assessments were documented. Complete blood count, glucose levels, liver function tests, urea, creatinine, albumin, red blood cell sedimentation rate, C-reactive protein (CRP)

levels, urine analysis, vitamin B12, and folate levels were analyzed.

Vitamin B12 levels were measured using the Electrochemiluminescence Immunoassay (ECLIA) method. The test was measured with the Cobas Vitamin B12 Kit (Roche Diagnostics, Mannheim, Germany) manufactured by Roche Diagnostics. The cut-off level for vitamin B12 deficiency was set at 200 pg/mL.

Urinary incontinence (UI) status was assessed by an experienced expert using three questions with yes or no answers (12). Stress urinary incontinence (SUI) was diagnosed based on the answer to the question, "During the past 12 months, have you leaked urine while coughing, lifting heavy objects, or exercising?" Urge urinary incontinence (UUI) was defined based on the answer to the question, "During the past 12 months, have you leaked urine with a sudden urge to urinate?" Other types of incontinence were determined by the question, "During non-physical activities have you leaked urine?" Individuals who responded positively to any question were considered to have urinary incontinence. Those who responded positively to both stress and urge urinary incontinence were classified as having mixed type urinary incontinence.

Statistical Analysis: Data were analyzed using IBM SPSS 26 software (IBM Corp. Released 2019). The Kolmogorov-Smirnov test was used to assess the normality of the distribution. For data that followed a normal distribution, an independent two-sample t-test was performed, while the Mann-Whitney U test was applied to data that did not follow a normal distribution. The Pearson chi-square test was utilized to compare categorical data across the groups. The relationship between laboratory measurements and B12 levels without normal distribution in the patient group was examined with Spearman's rho correlation coefficient. The results of the analysis are expressed as mean \pm standard deviation and median (minimum- maximum) for continuous variables, and as frequency (percentage) for categorical variables. A p-value of less than 0.05 was considered statistically significant.

Results

When comparing the age and gender distributions between the patient and control groups, no statistically significant difference was observed ($p=0.703$, $p=0.245$). The average age of the control group was 44.76 years, while the patient group had an average age of 43.6 years. The proportion of

Table 1: Analysis of Demographic, Clinical and Laboratory Results By Groups

Variables, mean \pm SD, median (min.-max.), %	Control (N=100)	Patient (N=109)	p
Age (year)	45.5 (18 - 62)	45 (18 - 62)	0.703#
Sex, n %			
Female	66 (66)	80 (73.4)	0.245 \square
Male	34 (34)	29 (26.6)	
Duration of Incontinence (Years)	-	2.37 \pm 2.14	
WBC ($\times 10^3$ / μ L)	6.475 (4.250 – 10.550)	7.240 (3.240 - 13.470)	0.057#
Neutrophil ($\times 10^3$ / μ L)	3.44 (0.74 - 7.04)	4.17 (1.46 - 10.67)	0.003#
HGB (g/dL)	13.6 (7.8 - 17)	13 (9 - 17)	0.119#
PLT ($\times 10^3$ / μ L)	254.5 (115 - 2060)	264 (123 - 440)	0.703#
Urea (mg/dL)	25 (12 - 48)	25.5 (14 - 55)	0.405#
Creatinine (mg/dL)	0.78 (0.49 - 1.16)	0.7 (0.4 - 1.2)	0.003#
Glucose (mg/dL)	98 (68 - 193)	92 (72 - 4100)	0.004#
Alb (g/dL)	4.5 (3.8 - 5.29)	4.3 (0.7 - 5.2)	0.001#
ALT (U/L)	23 (8 - 110)	19 (6 - 83)	0.003#
Vitamin B12 (pg/mL)	353.5 (197 - 777)	236 (119 - 560)	0.001#
Folate (ng/ml)	8.1 (1.67 - 24)	7 (2 - 24)	0.035#

#: Mann-Whitney U test, \square : Pearson's chi-square test, WBC: White blood cell, HGB: Hemoglobin, PLT: Platelet, Alb: Albumin, ALT: Alanine aminotransferase

Table 2: Examination of the Relationship Between Vitamin B12 And Laboratory Measurements In The Patient Group

	B12	
	r	p
Duration of Incontinence (years)	-0.045	0.640
WBC ($\times 10^3$ / μ L)	0.002	0.980
Neutrophil ($\times 10^3$ / μ L)	-0.061	0.558
HGB (g/dL)	-0.069	0.476
PLT ($\times 10^3$ / μ L)	0.076	0.434
Urea (mg/dL)	-0.095	0.330
Creatinine (mg/dL)	-0.028	0.772
Glucose (mg/dL)	-0.119	0.219
Alb (g/dL)	0.063	0.516
ALT (U/L)	-0.108	0.262
Folate (ng/ml)	0.054	0.621

r: Spearman's rho correlation coefficient. WBC: White blood cell, HGB: Hemoglobin, PLT: Platelet, Alb: Albumin, ALT: Alanine aminotransferase

females in the control group were 66%, compared to 73.4% in the patient group. Vitamin B12 levels were notably lower in the patient group than in the control group ($p=0.001$). Similarly, the folate levels in the patient group were significantly lower than those in the control group ($p=0.035$) (Table 1).

No statistically significant correlation was found between vitamin B12 level and incontinence duration ($r = -0.045$, $p = 0.640$), WBC ($r = 0.002$,

$p = 0.980$), neutrophil ($r = -0.061$, $p = 0.558$), hemoglobin ($r = -0.069$, $p = 0.476$), platelet ($r = 0.076$, $p=0.434$), urea ($r = -0.095$, $p = 0.330$), creatinine ($r = -0.028$, $p = 0.772$), glucose ($r = -0.119$, $p = 0.219$), albumin ($r = 0.063$, $p = 0.516$), ALT ($r = -0.108$, $p = 0.262$) and folic acid ($r = 0.054$, $p = 0.621$) levels (Table 2).

Discussion

The purpose of this study was to investigate the connection between urinary incontinence and vitamin B12 deficiency. These results indicate that individuals with urinary incontinence had considerably lower levels of vitamin B12 compared to the control group. Additionally, folate levels were also significantly reduced in the patient group when compared to the control group. These findings indicate that deficiencies in these important nutrients may be more common in individuals with urinary incontinence. In studies conducted on the treatment of urinary incontinence, preventive measures such as weight loss, smoking cessation, treatment of urinary tract infections, appropriate delivery methods and surgical interventions, as well as controlling diabetes, hormone replacement therapy, and reducing diuretic use are recommended. In addition, surgical options, drugs that reduce urine secretion and block muscarinic receptors, complementary treatment methods, and appropriate dietary practices are also included in treatment plans (13-15). An observational study of postmenopausal women found that artificial sweeteners increased the frequency of urinary tract infections (16). Tea consumption has been reported to increase excessive urinary incontinence, but studies on coffee consumption have yielded conflicting results (17,18). Chronic constipation is considered a risk factor for urinary incontinence. A diet enriched with foods with high fiber content and the consumption of raw fruits and vegetables are recommended. This study stated that a properly planned nutrition program reduces pelvic floor dysfunction and that physicians may need to recommend dietary treatment to women, including vitamin deficiencies, under the supervision of a dietitian (13,19).

Vitamin B12 deficiency may develop due to inadequate dietary intake, stomach diseases affecting the intrinsic factor, disorders affecting the terminal ileum, pancreatic insufficiency, and the use of certain medications. This deficiency is more common in older individuals, especially those with atrophic gastritis, increased autoimmune diseases, and multiple drug use (20). Age has been reported as a factor that increases the prevalence and severity of urinary incontinence. Large-scale studies on non-pregnant women reported that urinary incontinence affects 3% of women under 35 years of age, increases to 7% in women aged 55–64 years, and varies

between 38% and 69.9% in women aged 60 years and older (21,22). In the research carried out by Kesiktaş et al., it was found that vitamin B12 levels were lower in women with stress incontinence (23). In our study, vitamin B12 was found to be lower in patients with UI, consistent with literature.

Vitamin B12 is essential for the development and proper functioning of the nervous system (24). Insufficient levels of vitamin B12 can result in oxidative stress, calcium dysregulation, and disruptions in energy metabolism, which may cause neuronal shrinkage, cell death, and impaired neurotransmitter function (25). One study indicated that heightened oxidative damage and impaired neurological function due to B12 deficiency were linked to the onset of UI. B12 deficiency plays an important role in collagen synthesis and negatively affects the integrity of pelvic structures; in addition, increased oxidative stress and neurological dysfunction may contribute to the development of UI (26, 27). These results indicate that treating B12 deficiency may play a crucial role in the management of urinary incontinence.

Our study has some important limitations. Being retrospective and single-center prevents us from determining the causal relationship between B12 deficiency and urinary incontinence. In female patients, data such as parity, height, weight, BMI were not available and other possible confounding variables were not fully addressed, which may affect the results.

This study found a significant association between vitamin B12 deficiency and urinary incontinence. Vitamin B12 is vital for nerve function and collagen synthesis, and its deficiency can lead to both neurological and structural changes that lead to pelvic floor dysfunction and ultimately urinary incontinence. These results indicate that treating B12 deficiency may play a crucial role in the management of urinary incontinence.

Author Contributions: Concept/Design: HBP, BK; Data acquisition: OC, SY; Data analysis and interpretation: EK, SY; Final approval and accountability: HBP

Conflict of Interest: The authors declared that they have not received any conflict of interest and financial support.

Financial Disclosure: The authors have declared that they do not receive financial support.

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