

# Nöroşirürji Polikliniğinde Değerlendirilen 289 Hastanın Vitamin B12 Düzeylerinin Analizi

## Analysis of Vitamin B12 Levels of 289 Patients at a Neurosurgery Outpatient Clinic

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### Özet

Vitamin B12 yetmezliği periferik nöropatiye neden olabilir, periferik nöropati distal ekstremité parestezisi mevcudiyetinin en sık karşılaşılan sebebidir. Çalışmamızda hastaların serum vitamin B12 seviyeleri ve başvuru şikâyetleri incelendi. Tüm hastalar aynı klinisyen tarafından değerlendirildi. Beyin ve sinir hastalıkları cerrahisi polikliniğine başvurmuş olan hastaların dosyaları geriye dönük olarak incelendi. Ağrı ve/veya uyuşukluk/karınçalanma şikâyeti ile başvuran ve serum B12 düzeyi çalışılmış olan 289 hasta çalışmaya dahil edildi. Çalışmaya dahil edilmiş olan 289 hastanın 77 tanesinin serum B12 değeri 193 pg/ml değerinin altında tespit edildi (ort.157.82±27.45). Hastalardan 75'inin uyuşukluk/karınçalanma şikâyeti ile başvurmuş olduğu ve bunların serum vitamin B12 ortalamalarının 235.69±96.19 pg/ml olduğu, geri kalan 214 hastanın serum vitamin B12 ortalamasının ise 285.29±124.50 pg/ml olduğu tespit edildi. Bu değerler normal sınırlar içinde olmakla birlikte, iki ortalama arasındaki farkın önemli olduğu tespit edildi (t=3.136, p=0.002). Düşük serum vitamin B12 değeri her zaman dokudaki vitamin B12 yetersizliği ile birlikte değildir, aynı zamanda serum değerinin normal sınırdaki olması doku seviyesinin yeterli olduğu anlamına gelmez. Vitamin B12 eksikliği, kansızlık olmaması ve serum seviyesinin sınır değerler civarında olması durumunda dahi, duyu bozukluğu sebepleri arasında olabileceği düşünülmelidir.

### Abstract

Vitamin B12 deficiency may cause peripheral neuropathy and peripheral neuropathy is the most common cause of distal extremity paresthesias. The aim of this study was to determine the serum B12 level of the patients with complaints of pain and/or numbness/tingling and try to demonstrate the relation between them. Patients' files admitted to neurosurgery outpatient clinic were retrospectively analyzed. Serum vitamin B12 levels and the admission complaints of the patients were studied. A total of 289 patients with complaints of pain and/or numbness/tingling that serum vitamin B12 levels measured were included. All of the patients were evaluated by the same clinician. The serum vitamin B12 concentrations of 77 patients out of 289 were found to be below 193 pg/ml (mean 157.82±27.45). The total number of the patients with the complaint of numbness/tingling was 75 and the mean serum vitamin B12 level was 235.69±96.19 pg/ml, the mean serum vitamin B12 level of the remaining 214 patients was 285.29±124.50 pg/ml. Although these results were within the normal limits, the difference of the mean values of the two groups was found to be significant (t=3.136, p=0.002). The low serum vitamin B12 level does not always correlate with the tissue insufficiency and also it's serum level being normal does not indicate it's being sufficient at the tissues. Vitamin B12 deficiency should also be thought at the etiology of sensory disorder, especially if the radiological findings are normal, even though in the absence of anemia and serum level being at borderline.

**Anahtar kelimeler:** Vitamin B12 yetersizliği, nöropati, parestezi

**Key words:** Vitamin B12 deficiency, neuropathy, paresthesia

### INTRODUCTION

Vitamin B12 deficiency may cause myelopathy, encephalopathy, optic neuropathy and peripheral neuropathy. Myelopathy is known as subacute combined degeneration. Deficiency leads to dorsal column demyelination and lateral column demyelination may develop in the severe cases. It may also cause axonal degeneration or sometimes segmental demyelination in peripheral nerves. Symmetrical paresthesias in feet or hands may be the presenting symptom in the early stage of the disorder. The aim of this study was to determine the relationship between patient's admission complaints and serum B12 levels at Neurosurgery outpatient clinic.

### MATERIAL AND METHODS

Retrospective analyses of 289 patients were identified from medical records. The including criteria was patients admitting with complaints

of pain and/or numbness/tingling to neurosurgery outpatient clinic whom the serum vitamin B12 levels were measured. Serum vitamin B12 concentrations were measured by electrochemiluminescence immunoassay method (Roche Modular Analytics E170 (Elecsys Module) immunoassay analyzer). A cutoff value of <193 pg/ml was used to determine the low serum vitamin B12 level due to the reference level of the analyzer. Also serum folate level of 285 patients and Hemoglobine (Hb), mean corpuscular volume (MCV), white cell count (Leu), Platelet count (Plt) of 286 patients were measured. Out of 289 patients, x-ray was performed in 234, computed tomography (CT) in 121, magnetic resonance in 25 and electromyography (EMG) in 8 patients. In 19 patients none of the above was performed. All of the patients were evaluated by the same neurosurgeon. Statistical analyses were performed using the statistical software program SPSS. The t- test

**Table 1.** The relation between Hb, MCV, Plt, Leu and serum B12 level

	B12 (pg/ml)	n	Mean±SD	t	p value
Hb (gr/dl)	<193	76	13,85±2,09	1,234	0,218
	≥193	210	14,13±1,56		
MCV (fL)	<193	76	84,39±,15	0,367	0,714
	≥193	210	84,66±5,31		
Plt (/mm <sup>3</sup> )	<193	76	285,84±97,77	0,246	0,806
	≥193	210	283,23±71,39		
Leu (/mm <sup>3</sup> )	<193	76	7,23±2,19	0,732	0,465
	≥193	210	8,93±2,26		

The results are found to be insignificant at 76 patients serum vitamin B12 level below 193 and 210 patients above 193.

SD: standard deviation, Hb: Hemoglobine, MCV: mean corpuscular volume, Plt: Platelet, Leu: white cell count

was used to identify significant changes between two variables, if the variables were more than 2, one way anova test was used. A p-value lower than 0.05 was considered to be statistically significant.

## RESULTS

The serum vitamin B12 concentrations of 77 patients out of 289 were found to be below 193 pg/ml (mean vitamin B12=157.82±27.45). The complaints of these patients were pain for 46 patients (mean B12 level: 156.63±26.16), numbness/tingling for 9 patients (mean level B12: 157.12±32.93), pain and numbness/tingling for 22 patients (mean vitamin B12: 159.55±30.26), the difference of the mean values of the three groups was found to be insignificant (t=0.076, p=0.927). The total number of the patients with the complaint of numbness/tingling was 75 and the mean serum vitamin B12 level was 235.69±96.19 pg/ml, the mean serum vitamin B12 level of the remaining 214 patients was 285.29±124.50 pg/ml. The difference of the mean values of the two groups was found to be significant (t=3.136, p=0.002). 209 patients had normal skin sensation, their mean serum vitamin B12 level was 274.14±123.83 pg/ml, 66 patients had hypoesthesia, their mean serum vitamin B12 level was 271.11±105.11 pg/ml, 14 patients had paresthesia and their mean serum vitamin B12 level was 264.21±136.31 pg/ml, the difference of the mean values of the 3 groups was found to be insignificant (F:0.055, p:0.947). Although the difference of the groups was found to be insignificant (t:0.793, p:0.446), interestingly patients with normal reflexes had a mean serum vitamin B12 level 270.21±119.92 pg/ml, while 55 patients with reflex hypotonia had a mean serum vitamin B12 level 283.98±121.98 pg/ml. The number of patients that had normal x-ray findings was 93 with a mean serum vitamin B12 level of 264.81±115.72 pg/ml. The remaining 141 patients had spondylosis and their mean serum vitamin B12 level was 286.78±130.27 pg/ml. The difference of the mean levels of the two groups was found to be insignificant (t=1.319, p=0.188).

The mean serum vitamin B12 level of 23 patients that had normal CT findings was 261.39±85.55 pg/ml. On the other hand the mean serum vitamin B12 level of 98 patients that had spondylotic CT findings was 311.73±168.52 pg/ml. The difference of the mean levels of the two groups was found to be insignificant (t=2.039, p= 0.168). The 19 patients, that did not have any of the diagnostic tests, had a mean serum vitamin B12 level of 254.26±95.90 pg/ml. The mean serum vitamin B12 value of 8 patients that had EMG was 384.33±161.39 pg/ml. Five of them had nerve entrapment syndrome. Serum folate level was also measured at 285 patients, the mean value was 7.63±2.63 ng/ml at patients with the serum vitamin B12 level below 193 and, 8.50±3.17 ng/ml at patients with serum B12 level above 193. Both groups' folate levels were within

the normal limits, but the difference between the groups was found to be significant (t:2.112, p:0.036). Hb, MCV, Leu, Plt were measured at 286 patients, and the results are summarized at table 1, the results are found to be insignificant at 76 patients serum vitamin B12 level below 193 and 210 patients above 193. Among the 76 patients that had B12 level below 193, only 8 had anemia in whom 3 was normocytic and the remaining 5 was microcytic, none of the patients had macrocytic anemia.

## DISCUSSION

Total body vitamin B12 is 2 to 5 mg in an adult and almost 90 % of it is stored at the liver. As about 5 µg of vitamin B12 is used per day, deficiency may not develop for up to 5 years because of the excessive amount of storage. It is primarily obtained from meat and dairy products. The most important reason for deficiency development is intrinsic factor insufficiency, the other major causes are being a strict vegetarian, taking some drugs, being alcoholic and gastrectomy. Elderly people may have vitamin B12 deficiency up to 12-20% (1, 3, 4, 10). The well-defined two reactions which depend on vitamin B12 are conversion of L-methylmalonyl-CoA (coenzyme A) to succinyl-CoA and methylation of homocysteine to methionine. Folic acid and cobalamin play key roles in the metabolism of proliferating cells, deficiency leads to impaired DNA synthesis, also methylcobalamin is required in the central nervous system for myelin synthesis (2, 7). Some myeloproliferative and hepatic disorders may raise the concentration of transcobalamine 1 and 3, and cause a falsely normal serum vitamin B12 level. On the other hand despite serum level's being normal, tissue vitamin B12 deficiency may be present (2, 11). Vitamin B12 level may first fall in the neuronal tissues and later it may be reflected to its serum level (8). The neurologic complications of vitamin B12 deficiency is a combination of myelopathy and peripheral neuropathy: paresthesia, weakness, loss of vibration and position sense, visual impairment, changes in consciousness. Mild sensory neuropathy is the main neurological impairment in elderly people with vitamin B12 deficiency, and it may be reversible by treatment (5, 9). Although hyporeflexia or areflexia of the ankles is known to be the clinical hallmark of the peripheral neuropathy associated with vitamin B12 deficiency, by contrast the patients with reflex hypotonia had mean serum level of vitamin B12 higher than normal reflex group in our study. The values of the both groups were within the normal limits and this result is thought to be incidental. None of our patients had classical macrocytic anemia, it is a well-known entity that neurological complication may develop without any hematological abnormalities up to 25-85% of patients (6, 12). The mean vitamin B12 level of patients admitting with numbness/tingling was significantly lower than the patients whom admitting complaints were different. On the other hand complaints of the low B12 level group did

not correlate with this result. The low serum level of vitamin B12 does not always correlate with the tissue insufficiency and also its serum level being normal does not mean it's being sufficient at the tissues. Besides, there may be false positive and false negative measurements. The folate level was also significantly lower at the low B12 level group than the normal B12 level group but the mean value of the both groups were within the normal limits.

An important limitation of this retrospective study is the absence of the control group after B12 treatment and the demonstration of the improvement of the complaints with control serum vitamin B12 levels. The 26 % of patients having low serum vitamin B12 level may also be addressed to the Turkish people's serum vitamin B12 levels. Although the mean serum vitamin B12 level of patients that had abnormal x-ray and CT findings compared to normal ones did not have any significant difference, and also the eight patients that had EMG had normal mean serum vitamin B12 level, another limitation of the study is the symptoms are not correlated with the diagnosis of the patients, so it is possible that some of the patients had some obvious reasons for their symptoms like carpal tunnel syndrome or disc herniation. Also reason of the B12 insufficiency is not determined, some diseases which causes deficiency may also present with similar complaints. The important differential diagnosis of a patient's complaint for most of the Neurosurgeons is if it is something that needs to be operated or not. Imaging studies are often used for the differential diagnosis. The importance of this study is not showing the relation between B12 deficiency and peripheral neuropathy but to simply try to make remember that at least some part of the patients admitting to Neurosurgery outpatient clinic may have B12 insufficiency and some of the complaints may be related to the insufficiency.

Combining these results with the existing knowledge about the vitamin B12, it may be concluded that patients complaining from numbness/tingling, who do not have a significant neurological finding, should also be evaluated for B12 insufficiency. Even though serum vitamin B12 is normal, it may be addressed to tissue insufficiency at least for some cases. Low vitamin B12 level does not necessarily always cause neurological complaint and finding but also normal serum level does not always indicate normal tissue B12 level and exclusion of B12 insufficiency.

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