



Research Article

A Cross Sectional Analysis Vitamin B12 and Folic Acid Levels in Neurology and Psychiatry Outpatient's

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Summary

Objective: Vitamin B12 (VB12) and folic acid (FA) deficiencies may be subtle and unrecognized and cause various neuropsychiatric problems. Serum levels of VB12, FA and distribution patterns in a broad range of hospital adult population were investigated.

Methods: Cross-sectional analysis of laboratory results of VB12, FA during a year was made in a university hospital. Only the first measurements of the patients during this time frame were taken into analysis. The patients under 18 years were excluded. The laboratory results of 13875 patients VB12, FA levels were analysed. The mean levels of VB12, FA were analysed. VB12 and FA levels in different age groups and gender were also studied. Three different levels of VB12 were also analysed.

Results: The overall mean level of VB12 (n=13875) and FA were 344.84 ± 184.44 pg/mL, and 8.76 ± 3.96 ng/mL respectively. Mean levels of VB12 were 350.77 ± 184.43 pg/mL, in females and 332.20 ± 183.84 pg/mL, in males whereas mean FA levels were 9.12 ± 3.99 ng/mL in females and 8.01 ± 3.78 ng/mL in males. VB12 and FA levels was significantly high in females ($p < 0.001$). Level of VB12 was significantly different in all age groups ($p: 0.0001$).

Conclusions: We believe that VB12 and FA deficiency should be considered in a primary care setting and it is easy to treat and prevents serious neurological and psychiatric complications.

Key words: Vitamin B12, folic acid

Nroloji ve Psikiyatri Polikliniğine Bařvuran Hastlarda Vitamin B12 ve Folik Asit Dzeylerinin Kesitsel ncelenmesi

zet

Amaç: Vitamin B12 (VB12) ve folik asit (FA) eksikliğine baėlı nropsikiyatrik tablolar sinsice geliřebilir. Bu nedenle, hastaneye bařvuran geniř bir eriřkin hasta grubunda VB12 ve FA'nın kan dzeylerinin incelenmesi planlandı.

Yntem: niversite hastanesi laboratuvarında bir yıl boyunca alıřılan VB12 ve FA dzeyleri kesitsel olarak analiz edildi. Bu zaman kesitinde incelenen kan dzeylerinden sadece ilk alıřılan deėerler deėerledirmeye alındı. 18 yařın altındaki hastaların sonuları alıřmaya alınmadı. Toplam 13875 hastanın VB12 ve FA dzeylerinin ortalama deėerleri, farklı yař gruplarında ve cinsiyete gre daėılımı ayrıca  farklı VB12 dzeyinde de incelendi.

Sonu: Ortalama VB12 (n=13875) ve FA deėerleri sırasıyla 344.84 ± 184.44 pg/mL, ve 8.76 ± 3.96 ng/mL olarak bulundu. VB12 dzeyi kadınlarda ortalama 350.77 ± 184.43 pg/mL, erkeklerde 332.20 ± 183.84 pg/mL olarak saptanıırken, FA ortalama dzeyi kadınlarda $9.12 \pm$

3.99 ng/mL, erkeklerde 8.01 ± 3.78 ng/mL olarak saptandı. VB12 ve FA düzeyleri kadınlarda anlamlı olarak yüksek bulundu ($p < 0.001$). VB12 düzeyleri incelenen üç yaş aralığında da birbirinden anlamlı olarak farklı saptandı ($p: 0.0001$).

VB12 ve FA eksikliğinin neden olduğu ciddi nörolojik ve psikiyatrik tabloların önlenmesi için öncelikle birinci basamakta araştırılması gerektiğini düşünüyoruz.

Anahtar Kelimeler: Vitamin B12, folik asit

INTRODUCTION

Vitamin B12 (VB12) and folic acid (FA) deficiencies cause various neurologic and psychiatric diseases, such as cerebrovascular symptoms, dementia and depression^(1,2,8,13,16). However, they may remain subtle and unrecognized. The prevalence of subclinical VB12 deficiency is more than it is expected⁽⁸⁾. The VB12 deficiency (VB12D) is high among elderly patients, the prevalence was found about 20 % in developed countries due to food-malabsorption syndrome⁽⁷⁾. There is a misbelief about VB12D that it may only occur in strict vegans and pernicious anemia patients, it made difficult early diagnosis⁽³⁾. VB12 deficiency rises up to 30- 40 % in institutionalized elderly patients⁽⁵⁾. Allen (2004) reported that 40 % of the population had deficient or marginal plasma levels of VB12 in USA⁽⁴⁾. The cause of VB12D is often due to the low intake of animal-source of food in underdeveloped countries, it starts in early life and persists following years⁽³⁾. The description of deficiency level of VB12 is debatable.

Although it is accepted as under 150 pmol/L (or 200 pg/ml) in adults, the value of under 220 pmol/L (or 300 pg/mL) has been suggested to supply adequately⁽⁶⁾. Lindenbaum (1994) has proposed a cutoff value of deficiency level as 258 pmol/L (or 350 pg/mL) for elderly people through the studies by more sensitive indicator methylmalonic acid (MMA) for VB12 and homocystein⁽¹²⁾. Thus the deficiency states rises up to 43 % in the elderly and 14-16 % in the ages between 20-59⁽⁴⁾.

We aimed to investigate the levels, the distribution of the patterns of VB12, and

FA related with age, gender and different clinics in a broad range of a hospital adult population.

MATERIAL AND METHODS

This study is a cross-sectional examination of laboratory results of VB12 and FA for a year (Jan 1 – Dec 31, 2007) in a university hospital in İzmir, Turkey. Only the first measurements of the patients during this time frame were taken into analysis. The patients under 18 years were excluded. The standardized reference range was 198-982 pg/mL for VB12 and 3.0-17 ng/mL for FA. Measurements above 1000 pg/mL for B12 were excluded which were regarded as a result of supplement use. The spreadsheet of the data included demographic variables such as age and gender, the name of the clinics, and individual values of VB12 and FA from central laboratory, which was then transferred into SPSS 11.0 program. Clinics which had referred the patients were categorized into four groups as neurology, psychiatry and hematology and other clinics. The frequency of the VB12 and FA levels were analyzed in three different age groups (18-44; 45-64; 65 +). VB12 levels were categorized as low (< 198 pg/mL), marginal level (199-300 pg/mL), normal (above 301 pg/mL) were also analyzed according to the above criteria. Competitive chemi-luminescent enzyme immunoassays (Siemens, Immulite 2500, LA, USA).were used to measure serum VB12, FA and Hcy levels. The study was approved by the local ethics committee.

Statistical analysis

The descriptive statistics were calculated as mean, median and standard deviations. T- test was used for the difference between

gender. One way ANOVA and Bonferroni post –hoc comparisons were conducted for the difference between clinics and age groups. Chi-square test was used for the grouped levels of VB12.

RESULTS

We have analyzed the laboratory results of 13875 patients. (9448 females, 4427 males) The overall mean level of VB12 (n=13875) and FA were 344.84 ± 184.44 pg/mL, and 8.76 ± 3.96 ng/mL respectively. The mean levels of VB12 were higher in females than in males (p=0.0001) similarly mean FA levels were higher in females than in males (p=0.001).

The mean levels of VB12 increased significantly between age groups and the

folic acid levels were also different between age groups although not showing a trend (p= 0.0001) (Table 2). Mean levels of both VB12 and FA were significantly lower in psychiatry and neurology clinics, compared to hematology and other clinics (Table 3).

When VB12 levels were taken as low (under 198 pg/mL), low- normal (199-300 pg/mL), normal (above 301 pg/mL) levels, the percentage of low level were found 16.9 % in patients who had been referred from psychiatry, 18.8 % from neurology, 17.8 % from hematology and 19.7 % from other clinics respectively. The normal level of VB12 was 43.5 % in psychiatry clinic, 45.6 % in neurology clinic, 48.2% in other clinic and 46.5 % in hematology clinic.

Table 1: Mean VB12 and FA levels in males, females and whole group.

	Number of patients	Mean VB12 level pg/mL	Mean FA level ng/mL
Males	4427	332.20 ± 183.43	8.01 ± 3.78
Females	9448	350.77 ± 184.43	9.12 ± 3.99
Total	13.875	344.84 ± 184.44	8.76 ± 3.96

VB12 and FA levels were significantly higher in females p:0.0001

Table 2: Mean VB12 and FA levels in different age groups studied

	Number of patients	Mean VB12 level pg/mL	Mean FA level ng/mL
Ages 18-44	4543	321.85 ± 160.14	8.29 ± 3.79
Ages 45-64	5504	342.24 ± 181.86	9.15 ± 3.90
Age 65 ↑	3828	375.87 ± 209.12	8.81 ± 4.19

Mean VB12 levels were significantly different in all age groups. p:0.0001

Table 3: Mean VB12 and FA levels in different clinics.

	Number of patients	Mean VB12 level pg/mL	Mean FA level ng/mL
Neurology clinic	3685	338.73 ± 182.70	8.67 ± 3.88
Psychiatry clinic	1046	333.06±172.85	8.28 ± 3.83
Hematology clinic	593	346.08 ± 190.36	8.86 ± 4.17
Other clinics	8551	348.83 ± 186.03	8.88 ± 4.00

p:0.0006 for all groups

p value for psychiatry and other clinics is p:0.045

p value for neurology and other clinics is p:0.028

Table 4: Distribution of low and marginal levels VB12

	VB12 level < 198	VB12 level < 301	VB12 level > 301
Neurology clinic number	693	1310	1682
of patients			
%	18.8 %	35.5	45.6
Psychiatry clinic number	177	414	455
of patients			
%	16.9	39.6	43.5
Hematology clinic	117	200	276
number of patients			
%	19.7	33.7	46.5
other clinics	1476	2956	4119
number of patients			
%	17.3	34.6	48.2

DISCUSSION

According to our knowledge, this is the first study in the Turkish population evaluating the VB12 and FA levels. Our results showed that mean level of VB12 in our study was just above the marginal level (344.84 pg/ ml) and FA level was in normal range (8.76 ng/ml) (Table 1). VB12 and FA levels were significantly higher in females. Higher level of VB12 and FA in females and mean level of FA were similar in a study done in primary care centers in Israel⁽¹⁴⁾. Contrary to Israel study, our study was not done in a primary care setting. On the other hand, since our health care system did not limit admittance to a

university hospital, our results may also be regarded as a primary care population. In our society, females generally use and have benefit from health care system more often than males in cities. FA levels in our study may be a reflection of the 'Mediterranean diet' including more vegetables and fruit in our region^(11,14). It was difficult to compare our mean VB12 and FA levels with other studies since the designs were quite different. Diet including more fruit and vegetable resulted in high FA levels in our group, compared to the Iranian study⁽¹⁵⁾ and the mean VB12 level in the same study was in the marginal level and it was lower than our study. Mean levels of FA and

VB12 was significantly low in men similar to ours in this study⁽¹⁵⁾.

VB12 and FA levels according to age groups were also investigated (Table 2). The lowest level of VB12 and FA were in ages 18-44. VB12 level in this age group is close to the marginal range. VB12 level was highest in age 65 and among age groups. Since this is a cross-sectional study and we do not know their first VB12 level when first admitted, it is more likely that older group received supplementation and these are their control levels.

As far as we know there was not any study analyzing VB12 levels according to referrals from clinics. Significantly low levels of VB12 were found in patients admitting to psychiatry and neurology clinics in our study (Table 3). The levels of VB12 in psychiatry and neurology clinics were also close to marginal level. Having a marginal level VB12 might explain patient's complaints since VB12D may manifest with subtle symptoms. The number of patients tested in neurology was more than 3 times higher than patients in psychiatry clinic.

The distribution of VB12 levels in clinics showed that nearly 1/4 of the patients were in deficiency state and 1/3 of patients were in the marginal level (Table 4). These VB12 levels might cause a significant health care problem. Restoration of VB12D is important since early diagnosis and early diagnosis of VB12D is valuable, because once axonal damage is established recovery will not occur⁽⁹⁾.

If homocysteine levels were analysed in our population, we could have correlated them with patient's VB12 level in order to find out the reflection of VB12 status. In VB12D, it is suggested that monitoring homocysteine levels may provide insight into the effectiveness of the treatment⁽¹⁾.

Mediterranean diet which dominates in our region might be one explanation of relatively low level of VB12 in our study. Low intake of meat products might be

another explanation which is common in developing countries. Advice against eating red meat for cholesterol control also might effect the low levels of VB12 especially in the age group above 45. Low levels in younger age group might be a reflection of unbalanced diet again low income⁽³⁾.

One of the limitations of our study is that the hospital laboratory data does not reflect general population. Therefore our comments regarding the nutritional habits of the population may not apply to this group. However our hospital although being a university clinic, serves more like a community hospital for the surrounding settlements as a primary care facility.

Another main issue is that we don't have the data on the supplement use of the patients. Since we took a cross-section of the data, some of our patients have applied for a control after using VB12 and some are being checked for the first time. In spite of the limitations, differences can still be observed between different groups of patients.

We believe that VB12 and FA deficiencies should be considered in a primary care setting especially for the elderly patient population. It is a significant cause for many neurologic and psychiatric symptoms, which is easy to diagnose and treat.

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