

## ASSESSMENT OF VITAMIN B12 AND FOLIC ACID DEFICIENCY IN EMERGENCY DEPARTMENT AS A CAUSE OF ACUTE PRESENTATION OF DIZZINESS

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### ABSTRACT

**Aims:** Dizziness is one of the most common complaints between patients referred to emergency department (ED). The spectrum of etiology is quite large and includes many unknowns, so clinicians confront huge challenges to approach in patients who for the first time refer to ED for dizziness. So far there have been inadequate investigating systematically Vitamin B12 and folic acid deficiency in ED as a cause of acute presentation of dizziness (APD) etiologic factors. In this study, we investigated whether vitamin B12 and folic acid deficiencies play a role of APD etiology.

**Material and methods:** The study was performed prospectively with 100 APD patients having the first attack and referring to emergency service with no treatment anywhere previously and a control group including 100 volunteer participants. Differences between two groups were compared by the independent two sample t test. Categorical variables were compared between two or more group using the Chi-square test.

**Results:** Mean vitamin B12 levels were  $243.01 \pm 100.1$  mg/dl in patients' group and  $411.38 \pm 145.6$  in control group. Mean folic acid levels were  $8.77 \pm 1.33$  mg/dl in patients' group and  $8.83 \pm 2.71$  in control group. Mean vitamin B12 level was lower in patient group than control group compared with each other and this difference was statistically significant ( $p < 0.05$ ). On the other hand, there was not any difference in folic acid levels. In 26.7% of patients having dizziness with vitamin B12 deficiency did not experienced megaloblastic anemia.

**Conclusion:** We suggest that especially vitamin B12 levels should be analyzed in patients who admitted to ED for APD.

**Key words:** Vitamin b12, folic acid, deficiency, dizziness, acute presentation, emergency departments.

Received February 18, 2014; Accepted May 19, 2014

### Introduction

Affecting about 20-30% of the general population, dizziness is one of the most common complaints between patients referred to emergency department (ED). Approximately 2.6 million people suffering from dizziness visits ED per year in the United States of America<sup>(1,2)</sup>.

The spectrum of etiology is quite large and includes many unknowns, so clinicians face huge challenges to approach in patients who for the first time refer to ED for dizziness. At the course of diagnose, the fact that there is no specific diagnostic algorithm may cause both waste of time and incorrect treatment<sup>(3)</sup>. Due to increased rates of imaging and laboratory tests usage, the cost of patients has raised and its burden composes 4% of national health fund per year<sup>(4)</sup>.

In our emergency practices, we face difficulties to determine etiology of patients who are first

time experiencing dizziness in their lifetime and referring to emergency service. This equation with many unknowns to be solved as soon as possible and the etiology underlying the disease process should be clarified immediately, thus time lost and cost increases may be reduced.

The patients often refer to ED with attacks of acute presentation of dizziness (APD), recurrent positional triggered dizziness, recurrent spontaneous attacks of dizziness, and chronic persistent dizziness<sup>(1,5)</sup>. There is a case report in literature related to paroxysmal positional vertigo caused by vitamin B12 deficiency<sup>(6)</sup>.

But we have not found any study investigating vitamin B12 and folic acid deficiency which leads to APD in ED yet.

In this paper, we investigated vitamin B12 and folic acid serum levels in patients who experienced acute onset of dizziness APD first-time admitted to emergency service.

**Material and methods**

This study was conducted between in February 2013 and June 2013 at academic ED with the approval of the local ethics committee.

The study was performed prospectively with 100 APD patients having the first attack and referring to emergency service with no treatment anywhere previously, and a control group including 100 volunteer participants. After informed consent approves of all the participants, 5 milliliters venous blood samples were obtained. Serum vitamin B12 (normal range 191-663 pg/mL) and folic acid levels (normal range 4.6-34.8 ng/mL) were analyzed with DXI-1800 Beckman coulter device and complete blood count (CBC), (normal range of hemoglobin 12-19 g/dl) and mean corpuscular volume (MCV), (normal range 80-100 fl).

The patients with dizziness having any treatment/or not previously, and those having syncope, cerebral pathology, vitamin B12 and folic acid replacement, hemodynamic instability, chronic illnesses and anemia were excluded to the scope of study. Data were analyzed using SPSS (version 15, SPSS, Inc., Chicago, Illinois, USA).

Categorical variables were described as frequency (percentage), mean  $\pm$  standard deviation were used for continuous parameters. Differences between two groups were compared by the independent two sample t test. Categorical variables were compared between two or more group using the Chi-square test. For all analyses, p value < 0.05 was considered statistically significant.

**Results**

The study was conducted with a patient group including 100 patients with dizziness and a control group including 100 volunteer participants.

The patient group's mean age was 43 years old (range: 16-74 year) and composed of 70 (70%) female, and 30 (30%) men. The control group's mean age was 39.7 years (range: 20-71 year) and composed of 66 (66%) female, and 34 (34%) men.

Patient and control groups were similar to each other according to gender and age differences (p > 0.05) (Table 1).

The patients group consists of 70% female and 30% men. Gender frequency distribution was statistically significant (p=0.000). A total 34% of the patients' ages were 34 years old or younger, and 66 (66%) number of patients' ages were 35 years old

or older. Age groups frequency distribution was statistically significant (p=0.01) (Table 2).

	Patient group (n=100)	Control group (n=100)	p value
Female/male, n	70/30	66/34	0.547
Age, year mean ( $\pm$ SD)	43 $\pm$ 15.10	39.7 $\pm$ 12.77	0.095
Vitamin B12 pg/ml, mean ( $\pm$ SD)	243.01 $\pm$ 100.1	411.38 $\pm$ 145.6	0.000
Folic acid ng/ml, mean ( $\pm$ SD)	8.77 $\pm$ 1.33	8.83 $\pm$ 2.71	0.83

**Table 1:** Patient-Control Group.

Patients with dizziness		Frequency (%)	p value
Age	$\leq$ 34	34 (34)	0.000*
	$\geq$ 35	66 (66)	
Gender	female	70 (70)	0.01**
	male	30 (30)	

**Table 2:** The range of demographic data of the patients with dizziness.

\*Nonparametric Chi-square test: \*16.00, \*\*10.24.

Mean vitamin B12 levels were 243.01 $\pm$ 100.1 mg/dl in patients' group and 411.38 $\pm$ 145.6 in control group. Mean vitamin B12 level was lower in patient group than control group compared with each other. This difference was statistically significant (p=0,000). Mean folic acid levels were 8.77 $\pm$ 1.33 mg/dl in patients' group and 8.83 $\pm$ 2.71 in control group. There were no statistically significant difference between groups (p=0.830).

Low vitamin B12 levels were determined 30 (30%) number in patients' group and 6 (6%) number in control group, whereas low folic acid level were 2 (2%) number in patients' group and 1 (1%) in control group. A total 10 of 36 (27.8%) participants who have low vitamin B12 levels in both patient and control groups, hemoglobin and MCV values were normal limits. A total 3 participants who have low folic acid levels, none of their hemoglobin and MCV values were normal limits. In A total 8 of 30 (26.7%) patients with low vitamin B12 levels, hemoglobin and MCV values found normal limits, and similarly in 2 of 6 (33.3%) volunteer participants with low vitamin B12, hemoglobin and MCV values were normal limits (Table 3).

CBC profile	Patient group		Control group	
	Vitamin B12 deficiency (n=30)	Folic acid deficiency (n=2)	Vitamin B12 deficiency (n=6)	Folic acid deficiency (n=1)
Normal Hb and MCV value	8 (26.7%)	-	2 (33.3%)	-
Hb < 12 gr/dl and MCV > 100 fl	22 (63.3%)	2 (100%)	4 (66.7%)	1 (100%)

**Table 3:** CBC profile of the patient and control group with vitamin B12 and Folic acid deficiency.

**Conclusions**

Dizziness is a nonspecific terminology used commonly by the patients to describe some symp-

toms such as feeling of the movement, light-headedness, vertigo, syncop, pre-syncope, and generalized weakness<sup>(1,7)</sup>.

The etiology of dizziness is various and may primarily result from neurologic, cardiovascular, metabolic, psychogenic and vestibular system events. Because pathophysiologically multiple processes play a role, the pathogenesis could have not been uncovered exactly.

A 40-80 % of cases underlying etiologic agent could not identify<sup>(8)</sup>. Dizziness may be come out by to be influenced of inner ear vestibular apparatus functions. The inner ear contains sensitive organs, even though its' circulation differ from systemic blood circulation via blood-labyrinth barrier, vestibular functions may be effected metabolic changes<sup>(9)</sup>.

Vascular damage and haemostatic changes of labyrinth is possible pathophysiologic reasons for dizziness. Some studies which are related to homeostasis demonstrated that hereditary and acquired thrombosis is active in pathogenesis of labyrinthine dysfunctions<sup>(10-13)</sup>. Folic acid and vitamin B12 deficiencies lead to an increase of both arterial and venous thrombosis risk<sup>(14)</sup>.

Hyperhomocysteinemia take places in vitamin B12 and folic acid deficiencies and lead to toxic injury to endothelium, an increase of platelet aggregation and low density lipoprotein per oxidation that may cause to injury in labyrinth vascular structures<sup>(15)</sup>. By this way, vitamin B12 and folic acid deficiencies may have a part in dizziness pathogenesis via an increase of homocysteine levels. According to our results, Vitamin B12 deficiency ratios were 6% in control group and 30% in patient group with dizziness respectively. In other words, vitamin B12 deficiency was more significant in patients than control groups do. This result supports role of B12 deficiency in APD etiology given upper sentences.

Folic acid deficiency prevalence is lower than vitamin B12 deficiency prevalence in general population. The prevalence of folic acid deficiency may differ by depending on used population groups and methodological differences. Folic acid deficiency has been reported as a rate of 1% to 24%<sup>(16)</sup>.

In this study, folic acid deficiency was solely determined in three patients with dizziness. No difference was found between patient group and control group according to folic acid values.

Dizziness is more frequent in female than male gender. The higher age the more increases of dizziness prevalence is seen<sup>(7,8,17)</sup>. Newman-Toker et al.<sup>(2)</sup> reported that the prevalence of dizziness peaks in

third decade and the increase goes on by age.

We founded that the dizziness much higher in the patients with older than 35 years old.

Our results are similar to literature knowledge.

Folic acid and vitamin B12 take role in some important biochemical reactions as co-factors for example DNA synthesis. These important co-factors are not synthesis in human body as dot they should be taken exogenous by foods. Folic acid presents at herbal and food of animal origin. Vitamin B12 is found high rate in food of animal origin such as liver, kidney, meat, egg, cheese, milk, and seafood<sup>(18,19)</sup>.

These vitamin deficiencies usually emerge as a result of poor nutrition, malabsorptions gestation, and rising requirement in childhood. Variations between regional cultural, social and economic factors could lead to differences between dietary habits, thus differences may be seen in vitamin B12 and folic acid levels in region by region<sup>(19)</sup>.

In our region, because of high pregnancy rate of younger aged women and the number of gestation, vitamin B12 and folic acid demands increase. In our study, we excluded female participants who are received supplemental vitamin B12 and folic acid replacement. It has been found out that vitamin B12 deficiency leads to impairment of hematologic, neurologic, psychiatric, gastrointestinal, dermatologic, and cardiovascular system on all age groups<sup>(20,21)</sup>.

In folic acid deficiency, the clinic picture is the same as vitamin B12 deficiency do except neurologic symptoms and signs, which some of these disorders are neural tube defects, hyper homocysteinemia, mood disorders, and megaloblastic anemia<sup>(22)</sup>.

Folic acid deficiency may cause to megaloblastic anemia similar to vitamin B12 deficiency, distinction between the two conditions could be done clinically, which there is not present neurologic findings in folic acid deficiency<sup>(23)</sup>.

Although we saw imbalance findings on all of the patients in the present study, the neurologic findings were not seen any patients with folic acid deficiency. Vitamin B12 levels may be important to identify underlying etiologic factor in patients referred to ED with neurologic symptoms such as APD, imbalance feelings, ataxia, and peripheral neuropathy. Folic acid and vitamin B12 deficiencies the most common cause of megaloblastic anemia.

A simple CBC screening may provide early diagnose and treatment of the diseases<sup>(24)</sup>. But studies in the literature indicated that while hematologic profile is normal limits, the clinic findings may be obvious in vitamin B12 deficiency<sup>(25,26)</sup>.

In 26.7% of patients having dizziness with vitamin B12 deficiency did not experienced megaloblastic anemia in this study.

Even the anemia had been not recognized in CBC screening; it is a situation that physicians of ED should keep in sight to be faced with the APD related to vitamin B12 deficiency. A major limitation of this study is that homocysteine could not be analyzed, because assay of homocysteine levels, which is require 10 to 12 hours hungriness period before process, wasn't used routinely in our emergency laboratory.

## Conclusion

The patients evaluated for APD in ED, for establishment of etiologic diagnose by using easy and cost effective a test, and planning of treatment soon after, may be effective management for dizziness. Thus we suggest that especially vitamin B12 levels should be analyzed in patients with vague symptoms as do APD.

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