Middle Black Sea Journal of Health Science / Mid Blac Sea J Health Sci **November 2024; 10(4): 322-330**

ORGINAL ARTICLE **DOI:** 10.19127/mbsjohs.1488963

Evaluation of Vitamin B12 deficiency Anemia in Geriatric Patients

Aslıhan Mete Yıldırım[1](ID), Funda Datlı Yakaryılmaz[2](ID)

[1]İnönü University, Faculty of Medicine, Department of Medical Education, Malatya, Turkey
[2]İnönü University, Faculty of Medicine, Department of Internal Medicine, Geriatrics, Malatya, Turkey

Received: 24 May 2024, Accepted: 25 October 2024, Published online: 30 November 2024

Abstract

Objective: In our study, we aimed to evaluate vitamin B12 deficiency anemia, macrocytosis rate and vitamin B12 values in patients over 65 years of age and compare them with those under 65 years of age groups.

Method: Retrospectively, A total of 8062 patients, 1213 over the age of 65 and 6849 under the age of 65, admitted between March 2019 and March 2024 were included in the study. The patients' hemoglobin, hematocrit, Mean corpuscular volume (MCV), White blood cell (WBC), Red cell distribution width (RDW), Platelet (PLT) values and vitamin B12 levels were examined. Patients were divided into two groups as age of 65 and over (geriatrics) and age below 65 (young-adults), and each group were divided into two groups in terms of anemia. Groups and subgropus were compared with each other.

Results: While the ratio of vitamin B12 deficiency anemia in geriatrics was 20.2%, in young-adults it was 8.3%. No difference was observed in vitamin B12 levels in terms of gender in both age groups significantly. With the roc analyses the cut-off value for vitamin B12 causing anemia in elderly patients was 327 pg/mL (AUC: 0.602, p≤0.001) with a sensitivity of 94.3% and specificity of 34.2%.

Conclusion: The fact that vitamin B12 levels that cause anemia in elderly patients are higher than in young-adult patients made us think that the usual limit values may need to be reconsiderated in geriatric population

Keyword: Elderly, geriatrics, vitamin B12, anemia, MCV

Suggested Citation Mete Yıldırım A, Datli Yakaryilmaz F. Evaluation of Vitamin B12 deficiency Anemia in Geriatric Patients. Mid Blac Sea Journal of Health Sci, 2024;10(4):322-330

Address for correspondence/reprints:

Aslıhan Mete Yıldırım

Telephone number: +90 (506) 914 22 40

E-mail: aslihanmy@gmail.com

INTRODUCTION

Anemia is defined as a decrease in hemoglobin (Hb) concentration as a result of a decrease in erythrocyte mass. (1). The lower limit value is 12gr/dl for women and 13.5gr/dl for men. Studies show that this gap between men and women closes with age (2). Anemia is categorised in various ways depending on the etiological factors. Classification according to mean corpuscular volume (MCV) is one of the most frequently used classification systems. Anemias are divided into 3 subgroups according to MCV value: macrocytic, microcytic and normocytic.

Elderly population or geriatric population is defined as those aged 65 and over (3). Conditions such as physiological changes related to aging, increased prevalence of chronical diseases, changes in fluid intake, nutritional status and lifestyle and polypharmacy causes complexity in the interpretation of laboratory results in elderly patients (4). Recently, the view that laboratory results of elderly patients should be interpreted from a different perspective than those of adult patients has become widespread (4-6).

Vitamin B12 deficiency, which is one of the main causes of macrocytic anemias in the elderly population, however the diagnosis is sometimes missed because the symptoms it causes can be confused with cognitive and physiological symptoms related to aging. (7). The cut-off values determined for vitamin B12 deficiency vary in studies (8). In the diagnosis of vitamin B12 deficiency, it is based on the measurement of metabolic indicators such as homocysteine and methylmalonic acid after demonstrating that the serum vitamin B12 level is less than 200 pg/mL (148 pmol/L) (9,10).

Macrocytic anemia is expected in vitamin B12 deficiency (11,12). In some publications, increased MCV is accepted above 100 fL, while in others 96 fL and above is accepted (13). However, studies showing that not all patients with vitamin B12 deficiency develop macrocytic anemia are also available in the literature (14). These studies were generally performed in the adult population and levels specific to elderly patients were not studied. In our study, we aimed to evaluate and compare vitamin B12 deficiency, macrocytosis rate, and vitamin B12 values that develop anemia differently for both age groups.

METHODS

Study Population

After the approval of ethics committee patients who applied to the Internal Medicine and Geriatrics outpatient clinic of Turgut Özal Medical Center between March 2019 and March 2024 with the diagnoses of "anemia" and "general examination" were retrospectively examined. Among the observations, those with the following diseases were excluded from the study:

- Chronic Kidney Disease

- Chronic liver disease

- History of liver or kidney transplantation

- Chronic obstructive pulmonary disease

- Cancer

- Inflammatory bowel disease

- Alzheimer's

- Rheumatoid arthritis

The files of patients diagnosed with diabetes were examined and patients using metformin were excluded from the study. Among patients diagnosed with anemia, those with iron deficiency anemia were excluded from the study. When patients with missing datas were excluded from the study; A total of 8062 patients, 1213 with the age of 65 and over and 6849 under the age of 65, were included in the study.

The patients were divided into two groups: under 65 years of age and aged 65 and over. Each age group was divided into two subgroups: those with anemia and those without anemia.

Anemia was diagnosed as follows.

Hb < 12 mg/dL in female patients

Hb < 13.5 mg/dL in male patients (2).

MCV value > 96 fL was considered high (13).

Laboratory evaluation

The patients' hemoglobin, hematocrit, MCV, White blood cell (WBC), Red cell distribution width (RDW), Platelet (PLT) values and vitamin B12 levels were examined. For the complete blood count (CBC) panel, blood samples were collected in dipotassium EDTA tubes and measured on the SYSMEX XN 1000 Haematology Analyser (Sysmex Corporation, Kobe, Japan). Vitamin B12 measurements were made on a Beckman Coulter UniCel DxI 800 (CA, USA) autoanalyzer. Results were reported as pg/L for vitamin B12.

Statistical analysis

Data were analysed using SPSS version 25.0 (IBM SPSS Statistics, IBM Corporation, Armonk, New York, USA) and continuous variables were expressed as mean ± standard deviation. Normality was confirmed via the Shapiro-Wilk test. Student t-test was used to compare normally distributed data and Mann-Whitney u test was used to compare non-normally distributed data. ROC analysis was performed to estimate the optimal cut-off value of vitamin B12 for the occurrence of anemia in both groups. P value < 0.05 was considered statistically significant.

This study was a case-control study that was designed according to the STrengthening the Reporting of OBservational studies in Epidemiology (STROBE) guide.

RESULTS

Patients were divided into two groups: under 65 years of age (young-adults) and 65 aged and over (geriatrics). Then, both age groups were

divided into 2 subgroups: those with anemia and those without anemia. The laboratory values of the groups are given in Table 1 as mean ± SD. Accordingly, there was a significant difference in vitamin B12, WBC, Hb, HCT MCV, PLT and RDW values between the subgroups under 65 years of age (p≤0.001). When geriatric patients are divided into 2 subgroups, there was a significant difference in terms of age, vitamin B12, Hb, HCT MCV and RDW values (p≤0.001).

While the ratio of vitamin B12 deficiency anemia in geriatric patients was 20.2%, the ratio of anemia in young-adults was 8.3%.

When looking at whether there were differences in vitamin B12 levels in the subgroups in terms of gender; it was observed that there was no significant difference in both the age groups (Table 2).

While the rate of increased MCV was 3.8% in patients under 65 years of age, this rate increased to 4.9% in patients with vitamin B12 deficiency anemia. While the rate of increased MCV was 15.1% in geriatric patients, this rate increased to 29.1% in patients with vitamin B12 deficiency anemia.

The ROC analyses examined vitamin B12 levels causing anemia in patients under and over 65 years of age. The cut-off value for vitamin B12 causing anemia in geriatric patients was 327 pg/mL (AUC: 0.602, p≤0.001) with a sensitivity of 94.3% and specificity of 34.2% (Figure 1). The cut-off value for vitamin B12 in patients under 65 years of age was 222 pg/mL with 76.03% sensitivity and 55.18% specificity (AUC: 0.694, p≤0.001) (Figure 2).

Table 1. Laboratory values of age groups in terms of anemia

	Age ≥ 65			**Age < 65**		
	Anemia + (n:245) (%20.2)	**Anemia – (n:968) (%79.8)**	***p***	**Anemia + (n:569) (%8.3)**	**Anemia – (n:6280) (%91.7)**	***p***
Age (year)	75 ± 6	72 ± 6	**≤0.001**	39 ± 12	38 ± 13	0.124
Vitamin B12 (pg/dL)	220 ± 87	298 ± 166	**≤0.001**	197 ± 109	282 ± 152	**≤0.001**
WBC (103u/L)	8.4 ± 17.6	7.5 ±2.1	0.143	7.0 ± 2.1	7.4 ± 1.9	**≤0.001**
Hb (g/dL)	11.08 ± 1.18	14.00 ± 1.21	**≤0.001**	11.25 ± 0.76	17.34 ±1.41	**≤0.001**
Htc (%)	35.42 ± 3.85	43.36 ± 3.49	**≤0.001**	35.34 ±2.36	43.91 ±3.78	**≤0.001**
MCV (fL)	90.84 ± 6.73	89.14 ± 5.43	**≤0.001**	85.49 ±4.75	87.63 ±3.761	**≤0.001**
PLT (103u/L)	272.19 ± 102.23	263.05 ± 68.49	0.095	294.74 ±81.62	274.54 ± 64.47	**≤0.001**
RDW (%)	14.66 ± 1.84	13.56 ± 1.17	**≤0.001**	14.79 ± 1.84	13.12 ± 1.06	**≤0.001**

WBC: White Blood Cell, Hb: Hemoglobin, Htc: Haematocrit, MCV: Mean Corpucular Volume, PLT:Platelet, RDW: Red cell Distribution Width

Table 2. Vitamin B12 levels of age groups in terms of anemia

	Vitamin B12 levels (pg/dL) Age ≥ 65			**Vitamin B12 levels (pg/dL) Age < 65**		
	Female	**Male**	***p***	**Female**	**Male**	***p***
Anemia +	213 ± 87 (n:162)	232 ± 87 (n:83)	≤0.099	196 ± 104 (n:519)	215 ± 150 (n:50)	0.240
Anemia -	*296 ± 163* (n:619)	302 ± 171 (n:349)	0.571	283 ± 151 (n:4109)	281 ± 152 (n:2171)	0.580

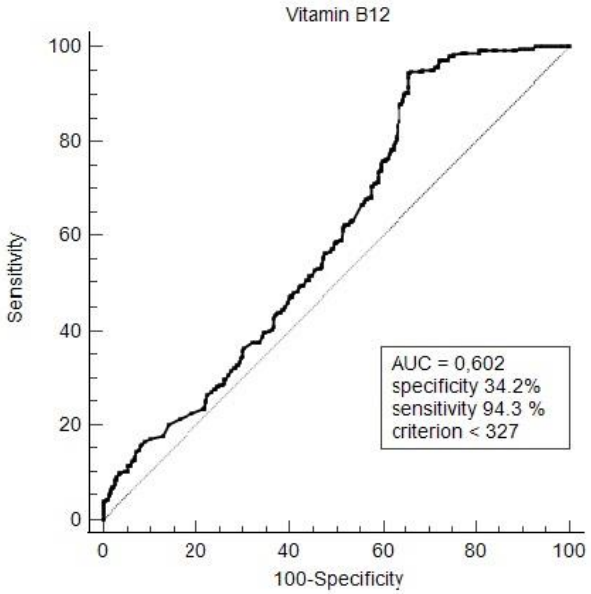

Figure 1. Vitamin B12 cut-off value causing anemia in the over 65 age group

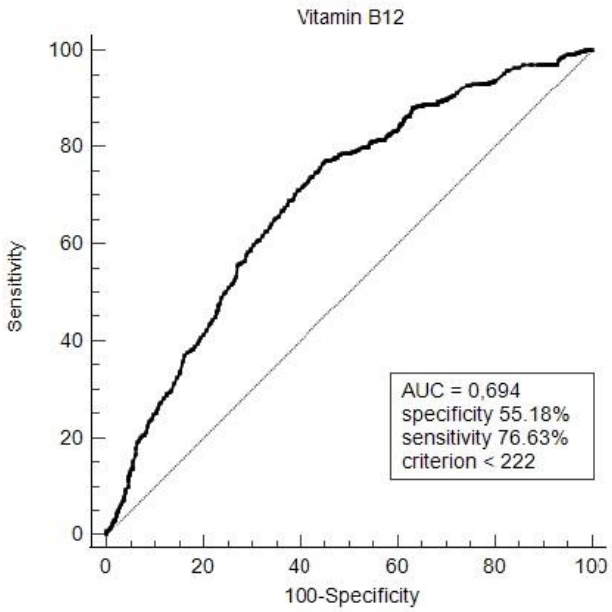

Figure 2. Vitamin B12 cut-off value causing anemia in the below 65 age group

DISCUSSION

The research study aimed to investigate and compare the prevalence of vitamin B12 insufficiency, the incidence of macrocytosis, and the particular vitamin B12 levels that result in anaemia in two different age groups, with a view to comparing younger individuals with older patients. The purpose of this study was to find any age-related variations in the manifestation and impact of vitamin B12 deficiency on hematological parameters, with an emphasis on the development of anemia and cellular features such macrocytosis.

We found that there was no significant difference in WBC and PLT values between the subgroups in geriatric patients. We thought the reason might be the physiological decline in platelet and leukocyte production with age (15).

The incidence of vitamin B12 deficiency anemia in patients over the age of 65 varying between 12% and 40% in the literature (16). The rate in our study was 20.2%. While this variability may be due to the effects of the number of patients, population and environmental factors, we think that the main reason is the difference in the cut-off value taken in each study.

We found that gender did not affect the development of vitamin B12 anemia in either age groups. There are several studies in the literature investigating the effects of gender on the development of anemia. (17,18). In these studies, the rate of anemia was found to be lower in elderly men than in elderly women (19).

Another finding of our study was that the MCV values were higher in the geriatric patients than in the patient group under 65 years of age. The MCV gradually increases with age, and in the 40-80 age group, women typically have lower MCV's than men (20,21). We also observed that the rate of increased MCV levels in patients under 65 years aged to be 3.8%. It is thought that MCV elevation is around 2.5% in the healthy population (22). In Turkey, this rate is estimated to be between 1.7-5% (23). Finding of our study was consistent with data in both national and international publications. We observed that the rate of MCV elevation without vitamin B 12 deficiency was 15.1% in the geriatric patient group. This was a higher rate than reported in previous studies (24). The main reason for this difference may be that malnutrition rates are higher in the region where our study was conducted. In addition, the possibility of concomitant folate deficiency could also explain this high rate. In our study, we observed that the cut-off value for vitamin B12 to cause anemia in people under 65 years of age was 222 pg/mL. For people 65 aged and over, this value was 327 pg/mL. While the accepted cut-off for low vitamin B12 in the literature is 200 pg/mL in past studies, more recent studies mention that even at levels of 350 pg/mL may be symptomatic (25,26). The

reason why higher levels of vitamin B12 cause anemia in the elderly may be due to poor functioning of peripheral blood cells as a result of a decline in the quality of bone marrow production, or it may be due to a decline in absorption with age, with higher levels of vitamin B12 reaching fewer target tissues.

Our study has some limitations. The first of these is that our study is retrospective. Another limitation is that metabolites such as homocysteine, methylmalonic acid and cobalamin levels were not measured in vitamin B12 deficiency diagnose. In addition, one of the limitations is that the patients' alcohol use status was not reviewed. Another limitation is that folate levels, another cause of macrocytic anemia, were not assessed in all patients.

CONCLUSION

Vitamin B12 levels change with age. The fact that vitamin B12 levels that cause anemia in elderly patients are higher than in young-adult patients made us think that the usual limit values may need to be increased, especially in the evaluation of patients aged 65 and over. We think that further studies are needed to enlighten the literature on this subject.

Acknowledgements : The authors would like to appreciate the patients participation in this study.

Ethics Committee Approval: Approval for this study was obtained from the İnönü University Non-Interventional Research Ethics Committee (2024/5381).

Peer-review: Externally peer-reviewed

Author Contributions: Concept: AMY, FDY, Design: AMY, FDY, Data Collection and Processing: AMY, FDY, Analysis and Interpretation: AMY, FDY, Writing: AMY, FDY,

Conflict of Interest: The authors declared no conflict of interest.

Financial Disclosure: The authors declared that this study has not received no financial support.

REFERENCES

1. Mulherin BP, Yeh M, Al-Adhami M, Dingli D. Normalization of Hemoglobin, Lactate Dehydrogenase, and Fatigue in Patients with Paroxysmal Nocturnal Hemoglobinuria Treated with Pegcetacoplan. Drugs R D. 2024;24(2):169-177
2. Ertilav M. What is the Target Hemoglobin Level Under the Scope of Current Issues? Turkish Clinics J Nephrol-Special Topics. 2012;5(2):57-62
3. Institute of Medicine (US) Committee to Design a Strategy for Quality Review and Assurance in Medicare; Lohr KN, editor. Medicare: A Strategy for Quality Assurance: Volume 1. Washington (DC): National

Academies Press (US); 1990. 3, The Elderly Population

4. Edwards N, Baird C. Interpreting laboratory values in older adults. Medsurg Nurs. 2005;14(4):220-9; quiz 230. PMID: 16206892.
5. Coskun A, Sandberg S, Unsal I, Serteser M, Aarsand AK. Personalized reference intervals: from theory to practice. Crit Rev Clin Lab Sci. 2022;59(7):501-516.
6. Fischbach, F.T., Fischbach M., Stout K. (2021). A manual of laboratory and diagnostic tests (11th ed.). Philadelphia: Lippincott
7. Elkıran T, Çelebi H. Determination of Laboratory and Clinical Findings in Patients with Megaloblastic Aanemia. Fırat Medical Journal 2001;6: 534-9.
8. Kara İH, Kandiş H, Bahçebaşı T, Köylü OK, Sayın S, Demirin H et al. Evaluation of Elderly Patients at Check-Up Polyclinics for Anemia, Serum Folate and Cobalamin Levels. Turkish Journal of Biochemistry–Turk J Biochem 2010; 35 (4): 350–355.
9. Klee GG. Cobalamin and folate evaluation: measurements of methylmalonic acid and homocystein vs vitamin B12 and folate. Clin Chem 2000;46:1277-83.
10. Andrès E, Perrin AE, Kraemer JP, Goichot B, Demangeat C, Ruellan A, et al. Anémies par carence en vitamine B12 chez le sujet âgé de plus de 75 ans: nouveaux concepts. À propos de 20 observations. Rev Med Interne 2000;21:946-55
11. Lahner E, Annibale B. Pernicious anemia: new insights from a gastroenterological point of view. World J Gastroenterol 2009; 15: 5121–8.
12. Oh RC, Brown DL. Vitamin B12 deficiency. Am Fam Physician 2003; 67: 979–86.
13. Hoffbrand V, Provan D. ABC of clinical haematology. Macrocytic anaemias. BMJ. 1997 8;314(7078):430-3.
14. Sun A, Chang JY, Wang YP, Cheng SJ, Chen HM, Chiang CP. Do all the patients with vitamin B12 deficiency have pernicious anemia? J Oral Pathol Med. 2016;45(1):23-7.
15. Bone marrow, thymus and blood: changes across the lıfespan. Aging Health. 2009;5(3):385-393.
16. Andrès E, Loukili NH, Noel E, Kaltenbach G, Abdelgheni MB, Perrin AE, et al. Vitamin B12 (cobalamin) deficiency in elderly patients. CMAJ. 2004;171(3):251-9.
17. Stopeck A. Links between Helicobacter pylori in - fection, cobalamin deficiency, and pernicious anemia. Arch In - tern Med. 2000;160: 1229-30.
18. Akbarpour E, Paridar Y, Mohammadi Z, Mard A, Danehchin L, Abolnezhadian F, et al. Anemia prevalence, severity, types, and

correlates among adult women and men in a multiethnic Iranian population: the Khuzestan Comprehensive Health Study (KCHS). BMC Public Health. 2022;22(1):168.

19. Özgümüş T. Anemia in the geriatric age group. Safer U, editor. Approach to Common Internal Problems in the Elderly. 1st Edition. Ankara: Turkish Clinics; 2021:.48-53.
20. Maner BS, Killeen RB, Moosavi L. Mean Corpuscular Volume. 2024 Mar 21. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan–. PMID: 31424859.
21. Lee JY, Choi H, Park JW, Son BR, Park JH, Jang LC, et al. Age-related changes in mean corpuscular volumes in patients without anaemia: An analysis of large-volume data from a single institute. J Cell Mol Med. 2022;26(12):3548-3556.

    doi: 10.1111/jcmm.17397. Epub 2022 May 22.
22. Hoffbrand V, Provan D. ABC of clinical haematology. Macrocytic anaemias. BMJ 1997;314:430-433
23. Ozkur M, Benlier N, Yilmaz M. Drug-Induced Macrocytosis. Yilmaz M, editor. Macrocytic Anemias. 1st Edition. Ankara: Turkish Clinics; 2019:.27-33.
24. Nagao T, Hirokawa M. Diagnosis and treatment of macrocytic anemias in adults. J Gen Fam Med. 2017;18(5):200-204.
25. World Health Organization. Nutritional anemias. Report on a Scientific Group. World Health Organ Tech Rep Ser. 1968;s: 405.
26. Lindenbaum J, Healton EB, Savage DG, Brust JC, Garrett TJ, Podell ER. et al. Neu - ropsychiatric disorders caused by cobalamin deficiency in the absence of anemia or macrocytosis. N Engl J Med. 1988:318:1720–8