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THE RELATIONSHIP BETWEEN NUTRITIONAL STATUS, ANEMIA AND OTHER VITAMIN DEFICIENCIES IN THE ELDERLY RECEIVING HOME CARE

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Abstract: *Aim:* The aim of this study was to evaluate the prevalence of anemia and other vitamin deficiencies among elderly home care patients and to evaluate the causes of anemia and effect of malnutrition as a contributing factor. *Methods:* Anemia was defined according to the World Health Organization. Hemogram, serum iron, iron binding capacity, ferritin and transferrin saturation values, serum vitamin B12, folic acid and vitamin D levels were evaluated. It was tried to differentiate as absolute iron deficiency anemia, anemia of chronic disease, anemia of unknown cause and vitamin B12 deficiency anemia. Malnutrition was evaluated by Mini Nutritional Assessment test. *Results:* Total of 472 patients (mean age 81,4±7,4 years) were included in the study. Anemia was detected in 179 (%37,9) patients, 22,7% of males and 45,5 % of female. Prevalence of iron deficiency anemia, vitamin B12, folic acid and vitamin D deficiencies were found 43%, 46%, 19% and 91% respectively. 22,8% of all patients were malnourished, 17,5% were under malnutrition risk. In patients with anemia 16,2% chronic disease anemia and 37,4% unknown anemia were detected. *Conclusions:* With or without malnutrition, iron deficiency anemia, vitamin B12 deficiency and vitamin D deficiency were common in the home care elderly patients.

Key words: Elderly, anemia, malnutrition, home care.

Introduction

The old age, which is the inevitable consequence of life is defined by the World Health Organization (WHO) as 65 years and above and its rate in the World population is increasing rapidly. According to the data of the World Health Organization, the number of people aged 60 years or older will rise from 900 million to 2 billion between 2015 and 2050 (moving from 12% to %22 the total global population) (1).

Anemia is frequently seen in the elderly and the incidence increases with age. Anemia in the elderly is associated with increased mortality and morbidity. Limited physical performance, the ability to perform activities of daily living, weakness, fatigue, fragility, falls, fractures, increase in the frequency and duration of hospitalization impairment of cognitive functions, depression and dementia have been shown to be associated with anemia (2).

The etiology of anemia in the elderly is multifactorial and complex. In the elderly without any other health problems other than anemia, when standard diagnostic procedures were performed, it was shown that at least one cause of anemia was detected in more than 91% of cases. However, it is not always possible to perform all investigations on anemia in the elderly (3).

In a large number of studies conducted in the literature with different methods, in different populations, the etiology was not clear in one third of the anemias seen in elderly patients. This is typically referred to as "Unexplained anemia", "Idiopathic anemia" or "Senile anemia" (3).

The pathophysiology of unexplained anemia is unclear in a large proportion of elderly anemic patients. Favored hypotheses include sex hormone deficiency, inflammation, endogenous erythropoietin deficiency with or without renal dysfunction (3).

The influence of malnutrition as one of the factors leading to anemia is greater than predicted (4). Malnutrition may lead to iron, vitamin B12 and folic acid deficiency, resulting in anemia. Iron deficiency anemia is the most common (4, 5, 6).

Serum ferritin is considered a first-line diagnostic tool not only due to its availability, but also because its plasmatic levels accurately reflect overall iron storage. The limit value for diagnosis is 12- 15 ng/ml, but if there is an accompanying chronic disease, the limit value is considered to be < 50 ng/ml (3, 8). While serum ferritin under 10-15 ng/ml has %99 of specificity in the diagnosis of iron deficiency, normal or elevated ferritin levels do not exclude iron deficiency anemia, since ferritin is an acute phase protein (6). Transferrin saturation is cheap and available in most laboratories and is quite suggestive of iron deficiency anemia when below 16%. However, inflammatory illnesses affect transferrin saturation and conclusions may be misleading if used as the sole marker (6).

The aim of this study was to evaluate the prevalence of anemia and other vitamin deficiencies among elderly home care patients and to evaluate the causes of anemia and effect of malnutrition as a contributing factor.

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Table 1
Distribution of patients with and without anemia according to some demographic characteristics

Patients characteristics		All Patients (n=472)	Anemia (n=179)	No Anemia (n=293)	P
Mean Age ± Standard deviation		81,4±7,3	82,0 ± 6,9	81,0 ± 7,5	0.409 [a]
Sex	Male (n, %)	158 (33.5)	36 (20.1)	122 (41.6)	<0.001 [a]
	Female (n, %)	314 (66.5)	143 (79.9)	171 (58.4)	
Main Diagnosis	Cardiovascular diseases (n, %)	82 (17.4)	24 (13.5)	58 (19.8)	0,024 [a]
	Cerebrovascular disease (n, %)	96 (20.3)	38 (21.2)	58 (19.8)	
	Orthopedic Diseases (n, %)	45 (9.5)	28 (15.6)	17 (5.9)	
	Oncologic Diseases (n, %)	9 (1.9)	6 (3.4)	3 (1.0)	
	Neurodegenerative Diseases (n, %)				
	140 (29.7)	45 (25.1)	95 (32.4)		
	Diabetes Mellitus (n, %)	45 (9.5)	16 (8.9)	29 (9.9)	
	COPD (n, %)	30 (6.4)	11 (6.1)	19 (6.5)	
	Senility (n, %)	23 (4.9)	10 (5.6)	13 (4.4)	
	Chronic Kidney Disease (n, %)	5 (1,0)	3 (0.6)	2 (0.4)	
Physical competence	Completely Immobile (n, %)	143 (30.3)	57 (31.8)	86 (29.4)	0.754 [a]
	Inside the house, to be able to move with wheelchair (n, %)	55 (11.6)	20 (11.2)	35 (11.9)	
	Walking at home with help (n, %)	274 (58.1)	102 (57.0)	172 (58.7)	
Malnutrition score	< 18 (n, %)	106 (22,5)	53 (50,0)	53 (50,0)	0,42 [a]
	18-24 (n, %)	69 (14,6)	23 (33,3)	46 (66,7)	
	25< (n, %)	297 (62,9)	112 (37,7)	185 (62,3)	
Nutrition Intake	PEG (Percutaneous endoscopic gastrostomy) (n, %)	6 (1,3)	2 (1,1)	4 (1,4)	0,312 [a]
	Nutrition support with formula (n, %)	71 (15,0)	34 (18,1)	37 (13,0)	
	Regular Oral (n, %)	395 (83,7)	152 (80,9)	243 (85,6)	

a. Chi-square test

Material and Method

In the retrospective, cross-sectional, descriptive study, anamnesis and examination forms, blood test results and Mini Nutritional Assessment forms were reviewed in the records of 729 patients over 65 years old who were enrolled in the home care unit of University of Health Sciences Ankara Dışkapı Yıldırım Beyazıt Hospital between 01.01.2016 and 31.12.2017. No sampling was performed since it was a descriptive study. Those who have previously used vitamin and mineral supplements, under the age of 65 and missing information about the research subject in their files, were left out of the study.

Patients were divided into two groups according to the WHO definition (Hb<13 mg/dl for men and Hb< 12 mg/dl for women) based on hemoglobin values as anemic and non-anemic ones. Anemic patients with serum ferritin < 50 ng/ml were defined as "Absolute Iron deficiency anemia". Serum iron, iron binding capacity and transferrin saturation values were evaluated in patients with ferritin > 50 ng/ml. Patients with anemia who have normal serum iron level (> 60 μ/dL), normal or decreased total iron binding capacity (TIBC) (250-450 μg/dL) and normal transferrin saturation (TS) (>16%) were defined as "Unknown anemia". Patients with ferritin values greater than 100 ng/ml, transferrin saturation decreased and TIBC decreased were evaluated as "chronic disease anemia" (9, 12). Those with serum vitamin B12 levels below 200 ng/ml were accepted as vitamin B12 deficiency and serum folic acid levels below 4 ng/ml were accepted as folic acid deficiency.10 Vitamin D levels below 30 ng/ml were defined as vitamin D deficiency (11).

Patients with anemia who have Mean Corpuscular Volume (MCV) values greater than 100 fl measured in complete blood count were defined as macrocytic anemia. Vitamin B12 deficiency anemia was defined if there was vitamin B12 deficiency with MCV elevation (10).

Malnutrition was evaluated by Mini Nutritional Assessment (MNA) test. Those with a test score of <17 were considered to be malnourished, those with a test score between 17 and 24 were at risk and >24 were considered normal.

Glomerular filtration rate (GFR) was measured using the modification of diet in renal disease (MDRD) formula (186 x

Table 2
Hematological and biochemical test values of all patients and groups separated according to hemoglobin values

Variables	n	All Patients		Anemia		No Anemia		P value
		Mean±sd	Median (min-max)	Mean±sd	Median (min-max)	Mean±sd	Median (min-max)	
Hemoglobin	472	12.4±1.8	12.5 (5.4-17.7)	10.6±1.2	10.8 (5.4-11.9)	13.5±1.1	13.3 (12.0-17.7)	<0.001[b]
MCV	472	88.7±37.1	87.7 (7.9-866.8)	85.2±10.1	85.4 (7.9-125.6)	90.8±46.3	88.6 (8.2-866.8)	<0.001[b]
MCH	472	28.6±2.6	28.7 (18.4-40.6)	27.8±3.1	27.8 (18.4-40.6)	29.1±2.1	29.1 (21.8-40.2)	<0.001[b]
Platelet Count	472	247.0±84.4	239.0 (16.0-639.0)	268.8±100.1	259.0 (16.0-639.0)	233.7±70.1	232.0 (17.0-583.0)	<0.001[b]
Leukocytes	472	7.6±3.9	7.2 (2.3-75.0)	7.3±2.8	7.0 (2.3-24.0)	7.8±4.5	7.4 (3.6-75.0)	0.036[b]
Serum Iron	472	57.8±27.8	54.0 (6.0-229.0)	45.6±27.1	39.0 (13.0-229.0)	65.3±25.5	64.0 (6.0-146.0)	<0.001[b]
Iron binding Capacity	471	234.6±70.7	225.0 (46.0-482.0)	243.3±86.2	227.0 (46.0-482.0)	229.2±58.8	224.0 (86.0-390.0)	0.389[b]
Transferrin Saturation	471	27.9±18.7	23.5 (3.1-163.6)	22.4±20.1	18.3 (3.8-163.6)	31.3±17.0	27.0 (3.1-98.0)	<0.001[b]
Ferritin	472	109.9±201.0	62.6 (3.6-2392.0)	133.7±274.1	63.4 (3.6-2392.0)	95.3±137.2	61.6 (5.9-1347.0)	0.988[b]
Vitamin B12	469	292.6±252.1	218.0 (2.6-1500.0)	328.8±305.5	232.0 (39.0-1500.0)	270.3±210.0	206.0 (2.6-1500.0)	0.233[b]
Folic Acid	470	9.1±43.0	6.2 (1.4-936.0)	7.4±4.8	6.2 (1.4-24.2)	10.2±54.4	6.3 (1.5-936.0)	0.873[b]
Vitamin D	471	14.1±12.5	10.4 (0.0-90.2)	13.0±12.1	9.5 (0.0-76.1)	14.7±12.7	10.5 (1.4-90.2)	0.024[b]
Albumin	459	3.6±0.5	3.6 (0.5-5.1)	3.4±0.5	3.5 (0.5-4.4)	3.7±0.4	3.7 (2.3-5.1)	<0.001[b]
Total Protein	465	6.8±0.7	6.8 (0.9-8.4)	6.6±0.8	6.7 (0.9-8.3)	6.9±0.5	6.9 (5.3-8.4)	0.003[b]
Cholesterol	469	181.2±43.3	177.0 (69.0-334.0)	170.5±36.9	166.5 (69.0-278.0)	187.8±45.6	184.0 (83.0-334.0)	<0.001[a]
AST	470	20.4±16.6	18.0 (1.0-318.0)	20.0±12.3	17.0 (1.0-109.0)	20.6±18.8	18.0 (9.0-318.0)	0.053b[b]
ALT	471	14.1±16.4	11.0 (2.0-254.0)	13.5±16.6	10.0 (2.0-194.0)	14.4±16.3	11.0 (4.0-254.0)	0.001[b]
MNA score	472	22.7±7.1	26.0 (3.0-30.0)	21.7±7.9	25.0 (3.0-30.0)	23.3±6.6	26.0 (4.0-30.0)	0.067[b]

a. Student-t test; b. Mann-Whitney U test

(plasma creatinine (mg/dl))-1,154 x (age)(year)-0.203 for men, for women the results were multiplied by 0.742. Glomerular filtration rate was expressed in ml/min/1.73 m2.

Statistical Analysis

All statistical analyses were performed using SPSS for Windows 11.5 software program (SPSS Inc., Chicago, IL, USA). Descriptive statistical methods in the evaluation of demographic data; frequency, percentage, mean, standard deviation was used. The compatibility of data with normal distribution was examined with the Kolmogorov-Smirnov test. Quantitative variables were stated as mean ± standard deviation (SD) and median (min-max), and categorical variables as number (n) and percentage (%). In the examination of a statistically significant difference between the categories of a qualitative variable with two categories in terms of a quantitative variable, the Student's t-test was used if the normal distribution assumption was met, otherwise the Mann-Whitney U test was used. The Chi Square test was applied to compare relationship between categorical outcomes. A value of $p<0.05$ was considered statistically significant.

Results

The mean age of the 472 patients included in the study was 81,4±7,4 years. Anemia was detected in 179 (%37,9) patients. Some demographic characteristics of patients with and without anemia are given in Table-1.

There was no significant difference between the groups with and without anemia in terms of age, primary diagnosis and mobility. Anemia was found to be significantly more frequent in women. When the patients' nutrition and MNA scores were compared, the difference was significant (p<0,001).

The hematological and biochemical test results for the anemic and non-anemic groups according to the hemoglobin values and for all patients are given in table 2.

When the groups with and without anemia were compared, Hb, MCV, MCH values, transferrin saturation were significantly different, but no significant difference was found between ferritin values (p=0.988). In patients with anemia albumin, total protein and cholesterol levels were statistically significantly lower. There was no significant difference in vitamin B12 and folic acid levels whereas vitamin D levels were significantly lower in the anemic group. There was no significant difference in MNA scores between groups with and without anemia (P=0.067) (Table 2).

In our study, iron deficiency anemia was found in 43% (n:77) of the patients with anemia and chronic disease anemia was found in 16.2% (n:29). 1.1% of the patients had both iron deficiency and chronic disease anemia. Three patients with chronic disease anemia had oncologic diagnoses. Three patients with chronic disease anemia who had GFR under 30 ml/min, they were considered as anemia due to chronic renal failure. Three patients had vitamin B12 and folic acid

Table 3
Classification of 179 patients with anemia according to serum ferritin, transferrin saturation, total iron binding capacity, serum iron, vitamin B12, folic acid and MCV values

Variables	n	%
Absolute iron deficiency anemia:		
Hb<12 g/dL and Ferritin <50 ng/mL, Transferrin saturation < 16%	77	43
Chronic Disease anemia:		
Hb<12 g/dL and Ferritin >100 ng/mL and Transferrin saturation < %16 and TIBC < 250 μg/dL	29	16,2
Unknown (unexplained) anemia:		
Hb<12 g/dl, Ferritin >100ng/mL,Transfer.saturasyon > %16 TIBC (250- 450 μg/dL) normal range or decreased, no vitamin B12 and folic acid deficiency, MCV normal.	67	37,4
Chronic Disease anemia + iron deficiency anemia:		
Hb<12 g/dL , ferritin >100 ng/mL, Transferrin saturation <16% and TIBC >450 μg/dL, serum iron <60 μg/ml	2	1,1
Vitamin B12 and Folic acid deficiency anemia:		
Hb<12 g/dL, serum iron, TDBK, Ferritin ve transferrin saturation were in the normal ranges, MCV>100 fL, Vitamin B12<200 pg/mL, folat<4 ng/ml	3	1,7
Unspecified megaloblastic anemia:		
Hb<12 g/dL, MCV>100 fL. All other parameters were normal.	1	0,6

Table 4
The prevalence of iron deficiency anemia, vitamin B12 deficiency, folic acid deficiency and vitamin D deficiency in patients with normal, at risk of malnutrition and malnutrition according to MNA scores and statistical analysis

Variables		MNA Scores						p
		≤17		18- 24		>24		
		n	%	n	%	n	%	
Vitamin B12	Low	41	38.7	37	45.1	140	50.0	0,132[a]
	Normal	66	61.3	45	54.9	140	50.0	
Folic Acid	Low	30	28.6	12	14.6	48	17.0	0,019[a]
	Normal	75	71.4	70	85.4	234	83.0	
Serum iron	Low	67	63.2	37	45.1	159	56.2	0,046[a]
	Normal	39	36.8	45	54.9	124	43.8	
Vitamin D	Low	97	91.5	76	92.7	259	91.8	0,956[a]
	Normal	9	8.5	6	7.3	24	8.2	
Iron deficiency Anemia	Low	94	88.7	68	82.9	233	82.3	0,307[a]
	Normal	12	11.3	15	17.1	50	17.7	

a. Chi-square test

deficiency anemia, while one patient had both iron deficiency and vitamin B12 deficiency anemia. No anemia etiology could be detected in 37,4% (n:67) of anemic patients. Although all other parameters were normal in one patient, the MCV value was greater than 100 fl and it was thought to have macrocytic anemia for a different reason except vitamin B12 and folic acid deficiency (Table 3).

In the study group consisting of 472 patients, 218 (46%) patients had vitamin B12 deficiency, 90 (19%) patients had folic acid deficiency, 432 (91%) patients had vitamin D deficiency. In the anemic group consisting of 179 patients, vitamin B12 deficiency was found in 77 (43%) patients, folic acid deficiency in 35 (19%) and vitamin D deficiency in 167 (93,2%) patients.

Table 5
Values of patients grouped with MNA scores and ferritin levels

MNA Score	Ferritin Values			P*	r **
	≤50 ng/ml	51- 100 ng/ml	>100 ng/ml		
≤ 17 (n, %)	28 (26,4)	28 (26,4)	50 (47,2)		
18- 24 (n, %)	37 (53,6)	11 (15,9)	21 (30,4)	0,000	-0,177
>24 (n, %)	133 (44,8)	85 (28,6)	79 (26,6)		

*Pearson Ki-Kare ** Pearson Korelasyon Coefficient

According to the MNA scores, 22,8 % (n:107) of patients were malnourished, 17,5% (n:82) were at risk of malnutrition and 59,7 (n:280) were within normal limits.

There was a statistically significant relationship between MNA scores and folic acid level and serum iron level categorical variables (p<0,05). There was no statistically significant relationship between MNA scores and vitamin B12, vitamin D and iron deficiency anemia categorical variables (table 4)

However, there was a statistically significant relationship between MNA scores and ferritin levels (p<0.001; r= - 0.177). As MNA scores decreased, ferritin levels were increased. The values of the patients grouped according to the relationship between MNA scores and ferritin levels were given in table 5.

Discussion

In our study, the prevalence of anemia was found to be 37,9% in patients who received home care over the age of 65 years. Anemia was detected in 22,7% of males and 45,5 % of females. We could not compare our results with a similar study because our study was performed in people over 65 years of age who received home care. However, the incidence was found to be higher than the studies in the literature which determined 9,6% in the US, 14,2% in Italy, 17,4% in Poland and 21% in Austria in the similar age group (2). Thirty-four studies, with 85,409 individuals, using WHO criteria, yielded a weighted mean anemia prevalence of 17% (range 3% to 50%) (13). In our country, studies on the frequency of anemia in patients over 65 years of age are limited. Some of these studies were performed in hospitalized elderly patients and the prevalence of anemia was found 76,3% and 76,4% (14). In a study conducted in 20000 elderly patients in a university hospital in Austria, the prevalence of anemia was 13,8% in outpatients and 29,8% in inpatients (5). In a review of 45 studies, 4 studies were conducted in nursing home (n:1481) (7), in hospitalized patients (n:13,953), 34 in community dwelling elderly (n:69,975) and the prevalence of anemia was 47%, 40% and 12% respectively (13). In our study, considering the group consisting of elderly patients with chronic diseases and physical disabilities, it was seen that the prevalence of anemia was consistent with the rates determined in the elderly living in the nursing home or hospitalized.

When the patients with anemia were examined, it was found that the anemia caused by iron deficiency was the first etiological factor with 43%, the second cause was unknown anemia with 37,4% and the third with 17,3% of the chronic disease anemia. These rates were similar to those seen in the third National Health and Nutrition Examination Study in the United States which were three common causes of anemia in the elderly (15). In the other studies examined, the first three reasons that cause anemia in the elderly remain the same even if the ranking changes with respect to these three etiological factors (2, 3, 5). In socioeconomically developed populations, iron deficiency anemia is seen in lower rates. Causes of iron deficiency in these developed countries may be diseases causing blood loss, loneliness, depression, lack of appetite or cognitive dysfunctions. Because the fact that our county is a socioeconomically developing country and its nutritional deficiencies are seen more, it is thought that the rates of anemia due to iron deficiency are slightly higher.

Although there was no significant difference between groups with and without anemia in patients with malnutrition according to MNA scores, total protein, albumin, cholesterol, serum iron levels, transferrin saturation and vitamin D levels were significantly lower in the group with anemia suggest that malnutrition is a contributing factor to anemia.

It is believed that some unexplained anemia cases are actually undiagnosed myelodysplastic syndrome (MDS), especially because the probability of MDS increases with age and initially, apart from anemia, there may be no other hematological abnormalities (2, 4, 5).

Chronic diseases lead to functional iron deficiency through complex interactions of inflammatory cytokines on iron metabolism and erythropoietin production. Further tests such as hepcidin, erythropoietin, soluble transferin receptor or soluble transferin receptor/log ferritin rate are recommended for differential diagnosis. In both anemia of chronic disease and iron deficiency anemia, serum concentration of iron and transferrin saturation are reduced, reflecting absolute iron deficiency in iron-deficiency anemia and “hypoferremia” due to acquisition of iron by the reticuloendothelial system in anemia of chronic disease. While total iron binding capacity increases in iron deficiency anemia, it decreases in anemia of chronic disease. Ferritin is also an acute phase reactant. Quantitative assessment of marrow iron stores is the ” Gold standard”

for diagnostic accuracy, but clearly impractical for screening purposes (15). In our study, a negative correlation was found between ferritin values and malnutrition scores. The high ferritin values in the elderly with malnutrition may be related to the fact that ferritin is an acute phase reactant. In the elderly who were evaluated as three groups according to the MNA scores, no significant difference was found between these three groups in terms of iron deficiency anemia, vitamin B12 and Vitamin D deficiencies, indicating that malnutrition alone was not responsible. Multifactorial causes play an important role in the anemias seen in this age group.

There are some limitations of our study. Differential diagnosis could not be made in some patients who may have a thalassemia carrier. Since C-Reactive Protein (CRP) showing acute or chronic inflammation could not be considered, this etiological factor could not be excluded in the anemia of unknown cause.

Conclusion

We found high incidence of "iron deficiency anemia" in our patients over 65 years of age enrolled in home care. Malnutrition, absolute iron deficiency anemia, other vitamin and mineral deficiencies when diagnosed, treatment is possible and can be corrected. We think that replacing these deficiencies would have a positive effect on the quality of life of patients with increased fragility, reduced function and high mortality and morbidity. However, it is not always possible to present the cause in individuals over 65 years of age with anemia and it is not possible with the existing routine evaluations and further investigations are required.

Message

Anemia in the elderly is multifactorial and complex. The diagnosis of unexplained anemia nearly one third of patients indicates further research to understand the causes of anemia in this age group.

Conflict of interest: The authors declare no conflicts of interest.

Ethical standars: The Approval of the Ethics Committee was obtained by decision number:51/04 on 11.06.2018.

Finding: Anemia was frequently diagnosed in this group of elderly patients (37.9%). There was no statistically significant relationship between anemia and malnutrition.

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