

RESEARCH ARTICLE

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Evaluation of Anemia Prevalence and Concomitant Diseases in Elderly Patients Applying to Family Medicine Polyclinic

ABSTRACT

Objective: The aim of this study was to review current approaches by evaluating anemia, which is the source of many negativities in increasingly aging population and directly affecting the quality of life, and the conditions associated with it.

Methods: The population of the study consisted of patients over 18 years old who applied to Family Medicine polyclinic in Ordu University Training and Research Hospital between May 2018 and May 2019. According to World Health Organization (WHO) criteria, a hemoglobin value below 13 g / dl in men and 12 g / dl in women is defined as anemia. The patients were divided into three groups according to their mean erythrocyte volume (MCV) as microcyte (MCV <80), normocyte (MCV 80-100) and macrocyte (MCV>100).

Results: Four hundred one participants aged 65 and over were analyzed in detail. The mean age of all patients was 78.3±8.65 years. Anemia was detected in 237 (59.1%) of 401 elderly participants. Of the elderly anemic patients, 42.6% were women and 16.4% were men. Of the elderly patients, 8.8% had microcytic anemia, 87.8% had normocytic anemia, and 3.4% had macrocytic anemia. Of the elderly patients, 32.9% had chronic disease anemia, 2% had iron deficiency anemia, and 40.5% had chronic kidney disease anemia.

Conclusions: The study conducted shows that anemia is a more frequent and greater problem than predicted in elderly patients admitted to an outpatient clinic. When the underlying cause is identified and treated, dramatic improvements can be achieved in the quality of life and life span of the elderly.

Keywords: Anemia, Geriatrics, Chronic Diseases, Family Medicine.

Aile Hekimliği Polikliniğine Başvuran Yaşlı Hastalarda Anemi Sıklığı Ve Eşlik Eden Hastalıkların Değerlendirilmesi

ÖZET

Amaç: Bu çalışmamızdaki amacımız, giderek yaşlanan nüfusumuzda birçok olumsuzlukların kaynağı olan ve yaşam kalitesini doğrudan etkileyen anemi ve ilişkili olduğu durumların değerlendirilmesi ile güncel yaklaşımların gözden geçirilmesidir.

Gereç ve Yöntem: Araştırmanın örneklemini Ordu Üniversitesi Eğitim ve Araştırma Hastanesi Aile Hekimliği polikliniğine Mayıs 2018 - Mayıs 2019 tarihleri arasında başvuran 18 yaş üzeri hastalar oluşturmuştur. Anemi tanımı, Dünya Sağlık Örgütü (DSÖ) kriterlerine göre hemoglobin değerinin erkeklerde 13 g/dl, kadınlarda 12 g/dl altında olması ile değerlendirildi. Ortalama eritrosit hacmine (MCV) göre; mikrositer (MCV<80), normositer (MCV 80-100) ve makrositer (MCV>100) olmak üzere üç gruba ayrıldı.

Bulgular: 65 yaş ve üzeri 401 katılımcı ayrıntılı olarak incelenmiştir. Hastaların yaş ortalaması 78.3±8.65 idi. 401 yaşlı katılımcının 237'sinde (%59.1) anemi tespit edilmiştir. Yaşlı anemik hastaların %42.6 'sı kadınlar, %16.4'ü erkeklerden oluşmaktadır. Yaşlı hastalarda mikrositer anemi % 8.8, normositer anemi % 87.8, makrositer anemi % 3.4 bulunmuştur. Yaşlı hastaların %32.9'unda kronik hastalık anemisi, %2 demir eksikliği anemisi, %40.5 kronik böbrek hastalığı anemisi vardır.

Sonuç: Yaptığımız çalışma ayaktan polikliniğe başvuran yaşlı hastalarda aneminin tahmin edilenden daha sık ve daha büyük bir sorun olduğunu göstermektedir. Altta yatan nedeni tespit edip tedavi yapıldığında yaşlıların yaşam kalitesinde ve yaşam sürelerinde dramatik düzeltilmeler sağlanabilir.

Anahtar Kelimeler: Anemi, Yaşlılık, Kronik Hastalıklar, Aile Hekimliği.

INTRODUCTION

Anemia is a global health problem due to its high prevalence and the associated significant morbidity and mortality in the elderly adult population (1). Anemia is an important public health problem in the elderly and approximately one quarter of elderly patients are anemic. The control of hematopoiesis is impaired with aging (2). There is a decrease in bone marrow in parallel with other organ functions. As the aging hematopoiesis becomes more sensitive to stress, the reduced reserve capacity of other systems with the development of anemia becomes symptomatic (3).

According to WHO criteria, a hemoglobin value below 13 g / dl in men and 12 g / dl in women is considered as anemia (4). Due to the lack of a uniform definition of anemia, the prevalence of anemia reported in older adults varies widely in the literature. It has been reported that the prevalence of anemia in older adults ranges from 2.9% to 51% in men and from 3.3% to 41% in women (5).

Aging is a physiological process, and general health and well-being are affected by several reasons. It is a condition that affects the development and results of smoking, alcohol, drugs, diet, sedentary lifestyle, age-related biological changes and functional disorders. The causes of death in the population aged 65 and over are defined as cardiovascular disease, cancer, lung disease, stroke, Alzheimer's disease, diabetes, and nephritis, respectively. In the elderly, anemia is affected by the burden of additional diseases, functional capacity, cognitive status and life expectancy. The decrease in physical and mental functions can profoundly affect the life of an elderly person and result in loss of independent life in the community (6). Quality of life is reduced when anemia is associated with specific diseases rather than alone. The improvement in anemia affects the quality of life positively regardless of the underlying disease (7).

In older adults, anemia is associated with other physical function markers, including weakness, increased frailty, muscle weakness, and falls. Anemia shows worse prognosis in elderly patients with anemia, cardiovascular and other chronic diseases. Survival benefit has been reported with the treatment of geriatric anemia in studies (8).

Causes of anemia in the elderly are basically divided into three groups. These are anemia due to nutritional deficiency, chronic disease anemia and anemia of unknown cause. There is no reason in 15-25% of them (9). The causes of anemia in hospitalized elderly are considered as chronic diseases, unexplained anemias, iron deficiency, bleeding, chronic kidney disease, liver and endocrine diseases, vitamin B12 or folic acid deficiency. In the elderly patients who are outpatient, the causes of it are listed as unexplained anemia, chronic diseases, iron deficiency, kidney and liver failure, and endocrine diseases (10).

MATERIAL AND METHODS

The study was initiated after the approval of Ordu University Faculty of Medicine Clinical Research Ethics Committee (Date: 23/05/2019; Approval No: 2019-86). Files of 520 patients aged 18 and over who applied to Ordu University Training and Research Hospital Family Medicine polyclinic between May 2018 and May 2019 were scanned. The group with active malignancy and hemoglobinopathy was not included in the study.

Hemogram measurements were performed with Cell-Dyn Ruby device. Cobas-C 501 module was used for the analysis of routine biochemical parameters Blood Urea Nitrogen (BUN) (mg / dl), creatinine (mg / dl), C-reactive protein (CRP) (reference range:0-0,5:mg / dl), serum iron, total iron binding capacity (TIBC) (mcg / dl)]. Ferritin (reference range:30-400 µg / l), vitamin B12 and folate levels were analyzed by Roche Cobas E-601.

Hemoglobin values below 13 g / dl for men and below 12 g / dl for women were accepted in the definition of anemia according to the WHO criteria. Iron deficiency was defined as serum ferritin value <20 ng / dl or serum iron <40 µg / dl and transferrin saturation <15% when serum ferritin value > 20 ng / dl. Anemia due to chronic inflammation was defined as serum ferritin value > 100 ng / dl and CRP > 0.5. Anemia due to chronic kidney disease was defined as GFR <60 ml / min / 1.73 m² in the calculation of GFR using the Cockcroft-Gault formula in anemic elderly. It was accepted MCV <80 fl as microcytic anemia, MCV between 80-100 fl as normocytic anemia and MCV > 100 fl as macrocytic anemia in the evaluation of erythrocyte mass.

SPSS 20 program (SPSS Inc. Released 2009. PASW Statistics for Windows, Version 20.0. Chicago: SPSS Inc.) was used for statistical analysis of the findings obtained from the study. The compliance of continuous variables to normal distribution was examined using the Kolmogorov-Smirnov test. In order to define the population, variables determined to be unsuitable for normal distribution were specified as median (minimum-maximum), and categorical variables were specified as numbers and percentages. In cases where the parametric test assumptions of the data were not provided, the non-parametric "Mann-Whitney U" test was used. Categorical data were analyzed using "Chi-square significance test". A 95% significance level (or $\alpha = 0.05$ margin of error) was used to determine the differences in the analyzes.

RESULTS

Of 520 cases included in the study, a total of 401 of those 65 years and older were examined in detail. The mean age of all patients was 78.3±8.65 years. Anemia was detected in 237 (59.1%) of 401 elderly participants (p <0.001). The prevalence of anemia in the elderly was observed as 16% in men and 41.7% in women. The number of elderly

anemic patients was 237 (59.1%), and 66 of them were male (27.8%) and 171 of them were female (72.2%). When comorbid diseases were examined with respect to anemia status in the elderly, a

difference was observed in terms of the presence of anemia (p = 0.004). No difference was observed with respect to drug use status (p = 0.268) (Table 1).

Table 1. Distribution of Demographic Characteristics in the Elderly According to Anemia Status

		Anemia*		p**
		Absent (n=164)	Present (n=237)	
Gender	Female	102(62.2)	171(72.2)	0.035
	Male	62(37.8)	66(27.8)	
Concomitant Disease	Diabetes Mellitus	9 (5.7)	14 (6.3)	0.004
	Hypertension	59 (37.1)	46 (20.6)	
	Cardiovascular Disease	6 (3.8)	20 (9)	
	Chronic Kidney Disease	7 (4.4)	10 (4.5)	
	Cerebrovascular Disease	7 (4.4)	22 (9.9)	
Multiple diseases		71 (44.7)	111 (49.8)	
Drug use	No drug use	11 (6.9)	24 (10.8)	0.268
	Antiaggregant-anticoagulant	14 (8.8)	31 (13.9)	
	NSAID	3 (1.9)	6 (2.7)	
	ACE inhibitors, ARB	20 (12.6)	18 (8.1)	
	Other Antihypertensives	28 (17.6)	41 (18.4)	
	Multiple drugs	83 (52.2)	103 (46.2)	

* frequency (percentage),** Chi-square test, NSAID:Nonsteroidal antiinflammatory drugs, ACE inhibitors: Angiotensin-converting enzyme (ACE) inhibitors, ARB: angiotensin receptor blockers

Median age values differed with respect to the presence of anemia (p <0.001). While the median value was 74 for those with anemia, it was 82 for those without it. Median hemoglobin values varied according to the presence of anemia (p <0.001). While the median value was 13.7 in those with anemia, it was 11.4 in those without it. Median hematocrit values differed in terms of the presence of anemia (p <0.001). While the median value was 41.6 for those with anemia, it was 35 for those without it. Median values of MCV did not vary with respect to the presence of anemia (p = 0.713). While the median value was 88.5 in those with anemia, it was 88.3 in those without it. Median folate values did not differ according to the presence of anemia (p = 0.233). While the median value was 7.9 in those with anemia, it was 7.4 in those without it. Median values of vitamin B12 varied according to the presence of anemia (p = 0.002). While the median value was 315.2 in those with anemia, it was 378.1 in those without it. The median values of ferritin differed in terms of the presence of anemia (p = 0.044).

While the median value was 63.3 in those with anemia, it was 93.3 in those without it. Median values of iron varied with respect to the presence of anemia (p

<0.001). While the median value was 79.9 in those with anemia, it was 58.7 in those without it. Median TIBC values differed according to the presence of anemia (p <0.001). While the median value was 322.9 in those with anemia, it was 288.5 in those without it. The median values of transferrin saturation varied in terms of the presence of anemia (p <0.001). While the median value was 0.19 in those with anemia, it was 0.25 in those without it. Median BUN values differed with respect to the presence of anemia (p <0.001). While the median value was 16.2 in those with anemia, it was 20.2 in those without it.

Median values of creatinine varied according to the presence of anemia (p = 0.027). While the median value was 0.8 in those with anemia, it was 0.9 in those without it. Median estimated glomerular filtration rate (eGFR) values differed in terms of the presence of anemia (p <0.001). While the median value was 80 in those with anemia, it was 68.1 in those without it. The median values of CRP varied with respect to the presence of anemia (p <0.001). While the median value was 0.3 in those with anemia, it was 0.7 in those without it (Table 2).

Table 2. Comparison of Laboratory Values in the Elderly According to Anemia Status

	No anemia*	Have anemia*	Total	p**
Age	74 (65 - 95)	82 (65 - 100)	78 (65 - 100)	<0.001
Hemoglobin (g / dl)	13.7 (10.2 - 17.7)	11.4 (1.7 - 14.3)	12 (1.7 - 17.7)	<0.001
Hematocrit (%)	41.6 (32.8 - 54.6)	35 (20 - 308.8)	37.2 (20 - 308.8)	<0.001
MCV (fl)	88.5 (44.3 - 101.6)	88.3 (36 - 113.6)	88.4 (36 - 113.6)	0.713
Folate (µg/L)	7.9 (2.3 - 20)	7.4 (1.8 - 941)	7.7 (1.8 - 941)	0.233
Vitamin B12 (µg/L)	315.2 (50 - 1890)	378.1 (27.2 - 2000)	349.1 (27.2 - 2000)	0.002
Ferritin (µg/l)	63.3 (5.1 - 1822)	93.3 (6.8 - 1845)	72.6 (5.1 - 1845)	0.044
Iron (µg/dl)	79.9 (30.2 - 180.1)	58.7 (2.3 - 309.2)	67.2 (2.3 - 309.2)	<0.001
TIBC (µg/dl)	322.9 (128 - 3410.5)	288.5 (26.4 - 499.6)	305.8 (26.4 - 3410.5)	<0.001
Transferrin saturation	0.25 (0.02 - 0.69)	0.19 (0.01 - 1.72)	0.22 (0.01 - 1.72)	<0.001
BUN (mg / dl)	16.2 (7.2 - 43.6)	20.2 (5.6 - 95.2)	18.1 (5.6 - 95.2)	<0.001
Creatinine (mg / dl)	0.8 (0.1 - 8.7)	0.9 (0.3 - 5.8)	0.9 (0.1 - 8.7)	0.027
eGFR (ml/min/1.73 m ²)	80 (28 - 122.8)	68.1 (8 - 122)	73.4 (8 - 122.8)	<0.001
CRP (mg/dl)	0.3 (0 - 8.5)	0.7 (0 - 27.5)	0.4 (0 - 27.5)	<0.001

*median (min-max), **Mann Whitney U test; MCV: Mean corpuscular volume, TIBC:Total Iron Binding Capacity, BUN: Blood Urea Nitrogen, eGFR: Estimated glomerular filtration rate, CRP: C-reactive protein.

The distributions of gender, B12 deficiency and folate deficiency do not differ with respect to MCV categories in the elderly (p = 0.717). The presence of anemia varies according to MCV categories in the elderly (p = 0.033). In the association between erythrocyte mass and anemia, MCV was within normal limits (80-100 fl, normocytic) in 210 (87.8%), low (<80 fl, microcyte) in 19 (8.8%) and high (> 100 fl, macrocytic) in 8 (3.4%) of 237 anemic elderly (p = 0.033).

No significant association was observed between vitamin B12 and folate deficiency and

erythrocyte mass in the elderly examined. Although there were 45 participants with vitamin B12 deficiency and 9 with folate deficiency, there were no participants with MCV values > 100 fl (Table 3).

While 16% of young people had iron deficiency anemia and 8.3% of them had chronic kidney disease anemia, 32.9% of the elderly had chronic disease anemia, 2% of them had iron deficiency anemia, and 40.5% of them had chronic renal failure anemia. A significant difference was observed with respect to chronic disease anemia and chronic renal failure anemia in the elderly (p <0.001) (Table 4)

Table 3.Distributions in the Elderly according to MCV Categories

	MCV<80 fl (n=25)*	MCV:80-100 fl (n=367)*	MCV>100 fl (n=9)*	Total	p value**
Female	17 (68)	251 (68.4)	5 (55.6)	273 (68.1)	0.717
Male	8 (32)	116 (31.6)	4 (44.4)	128 (31.9)	
No anemia	6 (24)	157 (42.8)	1 (11.1)	164 (40.9)	0.033
Have anemia	19 (76)	210 (57.2)	8 (88.9)	237 (59.1)	
No B12 deficiency	23 (92)	324 (88.3)	9 (100)	356 (88.8)	0.475
Have B12 deficiency	2 (8)	43 (11.7)	0 (0)	45 (11.2)	
No folate deficiency	24 (96)	359 (97.8)	9 (100)	392 (97.8)	0.754
Have folate deficiency	1 (4)	8 (2.2)	0 (0)	9 (2.2)	

*frequency (percentage), ** Chi-square test
MCV: Mean corpuscular volume

Table 4. Anemia Classification

	Young*	Older*	p value**
Have CDA	0	78 (32.9)	<0.001
No CDA	48 (23.2)	159 (67.1)	
Have IDA	8 (16)	6 (2)	<0.001
No IDA	40 (84)	231 (98)	
Have CKD	4(8.3)	96 (40.5)	<0.001
No CKD	44 (91.7)	141 (59.5)	

*frequency (percentage), ** Chi-square test
CDA:Chronic Disease Anemia, IDA: Iron Deficiency Anemia, CKD: Chronic Kidney Disease

DISCUSSION

Anemia is defined as a hemoglobin value below 13 g / dl in men and below 12 g / dl in women by WHO. Anemia becomes an important health problem in the elderly population as hemoglobin values decrease with age. Anemia brings along many diseases in the elderly population. Conditions increasing in the anemic elderly can be stated as mortality, cardiovascular disease, impaired cognitive functions, decreased mobility, fall and fracture risk, hospitalizations and length of stay (6).

The prevalence of anemia is affected by many conditions. Anemia is observed more frequently in developing countries. According to WHO, it is seen at a rate of 14% in Europe and 25% in our country. The prevalence of anemia has been reported to be 1.9-14% in men and 15-64% in women in Central South America and Asian countries (11). Considering the criteria determined for the definition of anemia, the results obtained

vary according to the location of the study (community, hospital, polyclinic, nursing home, etc.) and the health status of the participants. In elderly individuals, the prevalence of anemia is 12% in the community, 40% in hospital admissions and 47% in nursing home residents (12). In the literature, the prevalence of anemia has been found at quite different rates in elderly individuals. There are studies on anemia in the elderly population in our country. The prevalence of anemia was found to be 30% in the study conducted by Coban et al. on 2100 patients aged 65 and over who applied to the internal diseases polyclinic (13). Similarly, the prevalence of anemia was observed to be 32.5% in the study performed by Erkan et al. on 501 patients aged 65 and over who applied to internal diseases polyclinic (14). It was detected in the study conducted by Sahin et al. on 521 patients aged 65 and over that the frequency of anemia was 63% (15). It was found the prevalence of anemia to be

59.1% in this presented study, similar to Sahin et al. The high number of elderly and comorbid patients and the special patient referral from other health units in the region because of the fact that our hospital is a medical school hospital may be the factors for the high frequency of anemia in this study.

Memisogullari et al. investigated the types of anemia in their study. Microcytic anemia at rate of 46.9%, normocytic anemia at a rate of 52.6% and macrocytic anemia at a rate of 0.5% were found in their study (16). In a study conducted by Sahin et al. on patients admitted to the emergency service, 521 patients aged 65 and over were evaluated. Of those with anemia in the study, 76.6% was normocytic, 14.0% was microcytic, and 9.4% was macrocytic (15). It was detected in this presented study that normocytic anemia was at a rate of 87.8%, microcytic anemia was at a rate of 8.8%, and macrocytic anemia was at a rate of 3.4%. This presented study is compatible with the literature in this aspect.

One third of anemia is due to nutritional deficiency. More than half of anemias due to iron, folate and B12 deficiency also occur in this way. It was reported in the study conducted by Guralnik et al., the frequency of anemia due to nutritional deficiency was 35% in the United States. As nutrient deficiencies, iron, B12 and / or folate are the most common ones. Iron deficiency can be seen alone or together with vitamin B12 and folate deficiency (17). It was observed in the study performed by Amin et al., low ferritin (serum ferritin <12µg / l) was at a rate of 3%, iron deficiency was at a rate of 2%, and iron deficiency anemia was at a rate of 1.2% (18). The frequency of B12 deficiency in elderly patients was found as 26.4% by Sandikci et al. and 43% by Emiroglu et al. (19). In this presented study, the frequency of B12 deficiency in elderly anemic patients was observed as 11.2%. We think that B12 deficiency is lower than the literature in our patients because of the supplements of vitamin B12 in the patients who we have followed up in our hospital.

Anemia is usually caused by only one cause (for example, iron deficiency in pre-menopausal women with heavy menstrual bleeding) in younger people, whereas anemia is often multifactorial in the elderly and reflects the typical multimorbidity of older people. This often makes it difficult to examine the mechanism that causes anemia in the elderly. For instance; iron deficiency in the elderly can be seen due to malnutrition, which is often aggravated by the use of multiple drugs, and malabsorption. Losses from the gastrointestinal system can be considered as the most important cause of iron deficiency anemia. Nonsteroidal anti-inflammatory drugs (NSAIDs), antiaggregants and anticoagulants cause gastrointestinal system

bleeding. With aging, the rate of use of acetylsalicylic acid and other antiaggregants and anticoagulants increases due to cardiovascular diseases. Consequently, gastrointestinal complaints and gastrointestinal bleeding increase (20). In this presented study, the rate of cardiovascular disease in anemic elderly was 9%, and 13.9% of the patients used antiaggregant and anticoagulants and 2.7% of them used NSAIDs.

Of anemic patients in the study conducted by Karakus et al., 19.8% used proton pump inhibitors (PPI), 4.5% used NSAIDs, 2.3% used aspirin, and 0.7% used NSAIDs and PPIs (21). In this presented study, 2.7% of the elderly patients used NSAIDs.

The morbidity profiles of chronic diseases were evaluated in 171 patients in the study performed by Tariq et al. Hypertension at a rate of 61.4%, anemia at a rate of 46.8% and diabetes mellitus at a rate of 34.5% were observed most frequently (22). In this presented study, diabetes mellitus was found in 6.3% and hypertension was found in 20.6% of elderly anemic patients.

In the study conducted by Yuksel et al., 714 patients who applied to the general internal medicine and geriatric polyclinics and were diagnosed with iron deficiency anemia as a result of the examinations were evaluated. Anemia was detected in 37.7% of men and 62.3% of women (20). It was detected in the study performed by Imdat et al. on 642 patients in the city of Van that the prevalence of anemia was 15.9%, of which 17.3% were women and 11.9% were men (23). Sahin et al. (2013) stated in their study conducted on patients applied to the family medicine polyclinic that the prevalence of anemia was 29.2% in men and 33.3% in women (15). In this presented study, the frequency of anemia in the elderly was observed as 16% in men and 41.7% in women.

National Health and Nutrition Examination Survey (NHANES) data was used to determine the prevalence of anemia in patients with CKD in 2007-2008 and 2009-2010. According to the data of the United States between 2007 and 2010, 14% of the population was found to have chronic kidney disease. Anemia was seen in 15.4% of patients with chronic kidney disease and 7.6% of the general population. Anemia was twice as common in patients with chronic kidney disease compared to the normal population (24). In a study conducted by Sezer SD et al. on the etiology of anemia in the elderly, inflammation was the first (54%), the second was CKD (30.6%), followed by iron deficiency anemia (29.9%), vitamin B12 deficiency (16.7%) and folate deficiency (14.7%), respectively (25). In this presented study, the rate of CKD in patients over 65 years of age was found to be 4.5%. It was found the rate of anemia due to chronic kidney disease as 23% in the elderly in this

presented study. We think that the different rates of anemia in CKD patients in our country and in the world are due to the fact that the etiology of kidney disease in geographical regions is specific to that region. The study has some limitations. The first limitation is that the study is conducted retrospectively based on the laboratory values. Therefore, it cannot be said with certainty whether the abnormal laboratory parameters are a chronic or an acute condition. The second limitation of the study is that it is hospital-based. The findings are limited to patients presenting to the polyclinic and do not determine the general population. We think that new multi-center prospective studies on this subject will be guiding in this regard.

CONCLUSION

Consequently, anemia is a frequent occurrence in patients over 65 years of age in Turkey. Anemia in elderly patients in the world and in our country requires a special approach in terms of etiology, treatment and precautions. In our study, the most common cause of anemia in patients admitted to the family medicine outpatient clinic was normocytic anemia, demonstrating that chronic disease anemia plays a key role, especially in elderly individuals. This study emphasizes the importance of anemia in elderly patients. In addition, we think that this study will contribute to the evaluation of possible etiological factors of anemia.

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