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RESEARCH

THE PREVALENCE AND CHARACTERISTICS OF ANEMIA IN GERIATRICS IN THE WEST BLACK SEA REGION, TURKEY

ABSTRACT

Introduction: The aim of this study was to determine the prevalence and characteristics of anemia in geriatric population, which has important implications.

Materials and Method: As part of the Melen Study 2187 people were examined. All participants were given a physical examination, medical history and laboratory examinations. Of this larger group, 430 participants aged 65 and above, the "geriatric group", formed the focus of the present study that evaluated the incidence and morphology of anemia.

Results: Of the 430 geriatrics, 138 (32.0%) were identified as anemic. The prevalence rate of anemia was found to be 28% in women and 36% in men. The etiologies of anemia were found to be iron deficiency anemia, 40.5%; anemia of chronic disease, 7.9%; renal anemia, 14.4%; and unexplained anemia, 36.9%.

Conclusion: We found that anemia has different characteristics in geriatrics that necessitate special approaches in terms of etiology, precautions and treatment. Our study shows that anemia in geriatrics in Turkey may constitute a more important problem than it was thought to be.

Key Words: Anemia, Iron Deficiency; Aged; Prevalence.

ARAŞTIRMA

TÜRKİYE'DE BATI KARADENİZ BÖLGESİNDE YAŞLILARDA ANEMİ PREVALANSI VE ÖZELLİKLERİ

ÖZ

Giriş: Çalışmanın amacı pek çok açıdan özellik gösteren yaşlı nüfusta anemi sıklığının ve özelliklerinin irdelenmesidir.

Gereç ve Yöntem: Bu amaçla Melen çalışması kapsamında 2187 kişi incelemeye alındı. 65 yaş ve üstü olan 430 katılımcı 'geriatri grubu' olarak çalışmanın odak noktasını oluşturdu ve fizik muayene, anamnez ve laboratuar tetkikleri ile anemi sıklığı ve morfolojisi incelendi.

Bulgular: Toplam 430 yaşlı katılımcının 138 inde (%32.0) anemi tespit edildi. Kadınlarda anemi sıklığı %28.0 ve erkeklerde %36.0 bulundu. Anemilerin %40.5'i demir eksikliği, %7.9'u kronik hastalık anemisi, %14.4'ü renal anemi ve %36.9'u açıklanamayan anemiler olarak değerlendirildi.

Sonuç: Aneminin yaşlı kişilerde genelden farklı özellikler taşıdığı görülmektedir ve etiyoloji, tedavi ve önlemler açısından özel yaklaşımlar gerektirmektedir. Yaptığımız çalışma Türkiye'de yaşlı hastalarda aneminin tahmin edilenden daha önemli bir sorun olabileceğini göstermektedir.

Anahtar Sözcükler: Anemi, Demir Eksikliği; Yaşlı; Prevalans.

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Introduction

Anemia is a common problem worldwide; however, it is of great importance in terms of prevention, diagnosis and treatment for special groups such as children, the pregnant and geriatrics.

Studies carried out on geriatrics have shown rates of anemia ranging between 3 and 61% (1,2). According to the Turkish Statistical Institute database there are 5.7 million people (7.5%) aged over 65 in Turkey and it is estimated that by 2050, 20.8% of Turkish people will be geriatric (3).

The aim of our study was to determine the prevalence and characteristics of anemia in independently living geriatrics and to draw attention to the importance of the matter.

Materials and Method

Study Population: The Melen study is a prospectively designed survey aiming to investigate the cardiometabolic risk factors of Turkish people. This study was carried out in May and June 2010, in the citizens of Yığılca town, which is in Düzce, North-east Turkey and has a population of 17,000 people living in the town center and 39 villages. Yığılca town, with an elevation of around 350 metres above sea level, has geological and social characteristics similar to those of West Black Sea region. Two thousand one hundred andeighty-seven adult participiants (1407 women and 780 men), who had been randomized and invited to the health service office, were examined by anamnesis, physical examination and laboratory tests, and were assigned to either the 'young group' or the 'geriatric group'. The geriatric group, consisting of 430 participants (236 women and 194 men) aged 65 and above, formed the main population of study. The study protocol was approved by the Ethics Committee of Duzce University and every subject signed a consent form.

Definitions: Anemia was defined as hemoglobin (Hb) level below 13 g/dl for men and below 12 g/dl for women, in accordance with World Health Organization (WHO) criteria (4).

Iron deficiency was defined as ferritin <20 ng/dl or serum iron <40 µg/dl and transferrin saturation (TS) <15%.

Normocytic or microcytic anemia accompanied by iron deficiency was defined as iron deficiency anemia (IDA) (5).

Anemia of chronic disease (ACD) was defined as anemia that does not meet the criteria for iron deficiency and that has serum iron <60 µg/dl and glomerular filtration rate (GFR) >30 ml/dk, along with diagnosed chronic inflammatory disease or elevated inflammatory markers (ferritin>100 ng/dl or high-sensitivity C- reactive protein (hsC-RP) >4mg/dl).

The Cockcroft-Gault Formula (6) was used to calculate GFR, and renal anemia was defined as anemia in which GFR<30 ml/min/1.73m^2 or normocytic and microcytic anemias that do not meet the criteria for IDA and ACD when GFR is between 60-30 ml/min/1.73m^2.

The reference intervals were set at 80 to 95 fl for mean corpuscular volume (MCV), 0.4 to 4 IU/ml for thyrotropin and 0.8 to 1.7 µg/dl for free thyroxine.

The cut-off levels were 200 pg/ml for vitamin B_{12} (cobalamin) and 2 ng/ml for folate. A combination of cobalamin and folate deficiency along with MCV>95 fl was defined as megaloblastic anemia.

Those conditions that could not be identified by the criteria mentioned above were considered as 'unexplained anemia'.

Monthly or less frequent meat consumption was considered as inadequate meat consumption.

Biochemical and Complete Blood Count Analysis: Ten milliliters of blood was drawn from the antecubital vein by applying minimal tourniquet force. 2 ml of blood was drawn into vacutainer tube containing 7.5% K3 salt of ethylenediaminetetraacetate (EDTA) and 8 ml of blood was drawn into a vacutainer tube without anticoagulant. Blood samples were allowed to clot for 20 minutes and then centrifuged for 10 min at 1500 x g. Sera were shipped within a few hours on cooled gel packs at 2-5^{0}C to Duzce University's central laboratory and kept in Eppendorf tubes frozen at ?80 °C until final analyses.

Complete blood counts were done using CELL-DYN 3700 SL analyzer (Abbott Diagnostics, Chicago, USA). Serum iron, total iron binding capacity (TIBC) and ferritin levels were measured with commercial kits using cobas 6000 auto analyzer (Roche Diagnostics GmbH, Mannheim, Germany). Serum cobalamin and folate levels were measured by the Siemens IMMULITE 2000 competitive chemiluminescent enzyme immunoassay method (CCEA).

Statistical Analyses: Statistical Package for the Social Sciences software (SPSS 12, Chicago, IL, USA) was used for analysis. Descriptive parameters were shown as mean ± standard deviation or in percentages. Two-tailed t-tests and Pearson's chi-square tests were used to analyze the differences in means and proportions between groups. Non-normally distributed variables were compared using Mann-Whitney U tests. A p value of <0.05 was considered significant.

Results

Anemia was diagnosed in 32% (n=138) of the geriatric group, compared to 24% rate of anemia in the young group (p=0.001). The average age of the geriatric group was 71±5 and 28% of women and 36% of men were identified as anemic in this group (p=0.07). In terms of such social factors as chronic diseases, diet and level of income, the young group and the geriatric group were significantly different (Table 1). In the geriatric group, mean Hb concentration was 12.5±1.3g/dl for women and 13.4±1.3 g/dl for men. Mean Hb concentration in the geriatric group was lower than in the young group (respectively 12.9±1.4 vs 13.1±1.6 g/dl, p=0.006). Although mean cobalamin level was higher in the geriatric group (young group 266±126 vs geriatric group 307.4±166 pg/ml; p<0.001), cobalamin deficiency was more frequent (Table 1).

Ninety seven (22%) geriatrics (58 female, 39 male) had iron deficiency; the difference, in terms of gender, was non-significant (60% women and 40% men, p=0.28). One hundred and six (24%) geriatrics, 51(48%) women and 55 (52%) men, had cobalamin deficiency (p=0.045). Folate deficiency was detected in 30 geriatrics (6%) (Figure 1). Despite the high frequency of deficiences, megaloblastic anemia was not detected.

There was no history of malignancy, chemotherapy, connective tissue diseases, inflammatory bowel diseases and gastrointestinal hemorrhage in the last 6 months in the anemic participants. There was no history of drug use that could have been responsible for anemia.

MCV values were within normal limits in 94 (68%), low in 43 (31%), and high in only one of the total 138 anemic geriatrics (p<0.001). There was no significant association between cobalamin or folate deficiency and MCV.

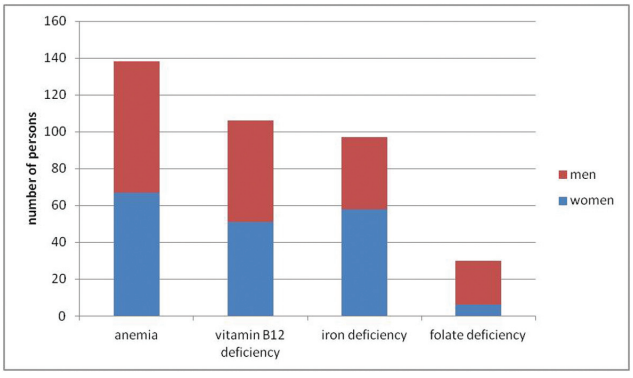

Figure 1— Distribution of anemia, iron, cobalamin, folate and gender in geriatric.

Table 1— Characteristics and Laboratory Parameters of Study Population.

	Geriatric Group (n=430)	Young Group (n=1757)	p
		Mean±sd or n (%)	
Age (year)	71.71±5.61	44.64±11.81	<0.001
Gender (women)	236 (54%)	1171 (66%)	0.001
Anemic	138 (32%)	427 (24%)	0.001
CKD	5 (1.2%)	7 (0.3%)	0.006
COPD	62 (14%)	97 (5%)	<0.001
Chronic medication	283 (65%)	683 (38%)	0.001
Adequate meat consumption	286 (66%)	1607 (91%)	0.001
Income level (YTL)	587.71±381.52	846.39±672.44	<0.001
Hemoglobin (12-18 g/dl)	12.9±1.4	13.1±1.6	0.006
MCV (80-95 fl)	84.1±6.8	82.7±6.6	<0.001
Iron (37 – 145 µg/dl)	79.48±32.93	80.61±36.04	0.56
Ferritin (15-150 ng/dl)	198.97±387.01	192.21±164.40	0.58
TS (15-50%)	22.64±9.75	22.10±10.6	0.33
TIBC (300-360 µg /dl)	361.22±67.69	379±68.57	<0.001
Cobalamin (191-663 pg/ml)	307.47±166.88	266.16±126.69	<0.001
Folate (4.6-18.7 ng/ml)	8.73±4.15	8.59±3.86	0.51

CKD: chronic kidney disease COPD: chronic obstructive pulmonary disease MCV: mean corpuscular volume RDW: red blood cell distribution width TS: transferrin saturation TIBC: total iron binding capacity.

Table 2— Comparison of Geriatrics in Terms of Iron and Cobalamin Deficiency.

	With Iron Deficiency (n=97)	Without Iron Deficiency (n=33)	p	With Cobalamin Deficiency (n=106)	Without Cobalamin Deficiency (n=324)	p
				Mean±sd or n (%)		
Age; year	71.8±5.9	71.62±5.54	0.68	71.81±5.28	7.65±5.80	0.81
Gender; women	58 (60%)	177 (53%)	0.28	51 (48%)	141 (43%)	0.045
Hemoglobin gr/dl	12.0±1.6	13.18±1.22	<0.001	12.93±1.59	12.94±1.32	0.96
MCV fl	81.0±6.5	85.22±4.79	<0.001	84.32±6.17	84.32±4.91	0.94
TS %	11.5±3.9	26.03±8.39	<0.001			
Demir µg/dl	46.4±17.7	89.4±29.76	<0.001			
Ferritin ng/dl	191±176	201±413.13	0.83			
Anemic	56 (57%)	82 (24%)	<0.001	37 (34%)	75 (23%)	0.56
Folate deficiency	6 (6.2%)	24 (7.5%)	0.67	7 (0.6%)	15 (0.4%)	0.94
Cobalamin deficiency	24 (25.0%)	80 (25.2%)	0.90			
Iron deficiency				24 (22%)	53 (16%)	0.9

MCV: mean corpuscular volume TS: transferrin saturation.

When the geriatrics with and without iron defficiency were compared, there were no significant differences in terms of gender, cobalamin, or folate levels, and also social factors such as level of income, living in a rural area and meat consumption (p>0.1). Unlike the other iron parameters, there was no significant difference between the means of ferritin levels between the two groups (191.1±176 vs 201.3±431 ng/dl; p=0.3) (Table 2).

When the geriatrics were grouped according to their cobalamin levels, the participants with low and normal cobalamin levels were similar in terms of Hb concentration, MCV, anemia frequency and meat consumption (p>0.5) (Table 2).

Three anemic geriatrics were identified with manifest hypothyroidism (free thyroxine<0.8 µg/dl). Two of them were identified as IDA and one as ACD. Anemia resulting mainly from hypothyroidism was not identified.

For the geriatrics with and without anemia, comparisons with respect to cobalamin and folat deficiency, hypothyroidism, the presence of type 2 diabetes, hypertension, chronic obstructive pulmonary disease (COPD) and hsC-RP level were not significant (Table 3).

The Hb concentration was over 10 g/dl in 92% and below 8 g/dl in 4% of anemic geratrics.

When the anemias were classified according to the dominant etiology, IDA was identified as the most common one (40.5%). The rate of renal anemia was identified as 14.4%, ACD as 7.9% and unexplained anemia as 36.9% (Figure 2).

Forty (78.4%) of the geriatrics with unexplained anemia had normocytic red cells and 11 (21.6%) had microcytic red cells. Macrocytic anemia was not identified in this group. Of the geriatrics with unexplained anemia, 5 had COPD, 2 had subclinic hypothyroidism (one had thyrotropin >10 IU/mL), and 1 reported alcohol consumption; these were factors that could be associated with anemia. Although they did not meet the criteria for ACD (since their serum iron levels were >60 µg/dl), in 9 geriatrics with unexplained anemia the hsC-RP levels were >4 mg/dl, (4 of them >10 mg/dl), and in 12, ferritin levels were >300 ng/dl. There was renal insufficiency (GFR<60 ml/dk) along with iron deficiency in 15, presence of inflammation markers (TS>15%, serum iron<60 µg/dl, and ferritin>100 ng/dl and/or hsC-RP>4 mg/dl) along with iron defficiency in 6, and renal insufficiency along with presence of inflammation markers in 3 of the anemic geriatrics. In 21% of all anemic geriatrics and 30% of anemic geriatrics with known etiology, there were multiple factors responsible for etiology. The anemia in 51 geriatrics, whose anemia etiology was not clearly identified, was considered to be unexplained anemia.

Discussion

Despite various studies on the prevalence and characteristics of anemia in geriatrics, it is difficult to compare their results since these studies contain differences in the definition

Table 3— Comparison of Geriatrics With and Without Anemia.

		Anemic (n=138)	Not Anemic (n=292)	p
			Mean or n (%)	
Gender, women		67 (48.5%)	169 (57.8%)	0.07
Age		72.8	71.1	0.004
Hemoglobin g/dl	women	10.9	13.1	<0.001
	men	12.0	14.2	
Iron µg/dl		67	85	<0.001
Ferritin ng/dl		183	206	0.5
Transferrin saturation %		18	24	<0.001
TIBC mcg/dl		373	355	0.01
Folate ng/ml		8.8	8.6	0.6
Cobalamin pg/ml		315	303	0.5
Income YTL		566	597	0.4
Diyabetes Mellitus and/or Hypertension		68 (49.2%)	160 (54.7%)	0.55
COPD (diagnosed)		21 (15.2%)	41 (14%)	0.7
CKD (diagnosed)		1 (0.7%)	4 (1.3%)	0.18
GFR<60 ml/dk		40 (28%)	45 (15.4%)	0.008
Iron deficiency		56 (40.5%)	41 (14%)	<0.001
Folate deficiency		10 (7.6%)	20 (6.8%)	0.84
Cobalamin deficiency		37 (26.8%)	69 (23.6%)	0.56
Manifest hypothyroidism (fT4<0.8 µg/dl)		3 (2.1%)	10 (3.4%)	0.49
Alcohol consumption (>20 gr daily)		4 (2.8%)	2 (0.6%)	0.07

TS: transferrin saturation TIBC: total iron binding capacity hsC-RP: high sensitive C-reactive protein COPD: chronic obstructive pulmonary disease CKD: chronic kidney disease GFR: glomerular filtration rate.

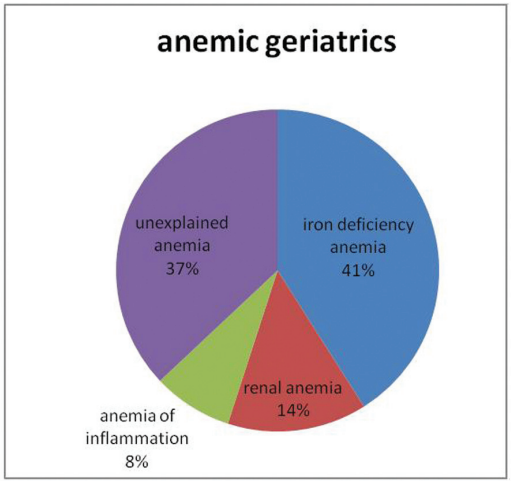

Figure 2— Distribution of etiology of anemia.

of anemia and in the characteristics of study populations. The rate of anemia (32%) was higher in our study than in similar studies. In NHANES III, an important study on this subject, the rate of anemia was 10.2% for elderly women and 11% for men (7). In 2000, Olivares et al. (8) from Chile found the rate of anemia to be 4.4% for women and 5.4% for men. Tettamanti et al. (9) in Italy found the rate of anemia to be 14%. In the Framingham heart study (10), 6.1% of men and 10.5% of women were reported to be anemic. In these studies, WHO criteria were used in the assessment of anemia and apparently healthy geriatrics living independently were studied.

Few studies have been conducted in Turkey on the anemia in geriatric population. Çoban et al. (11) from Antalya reported the rate of anemia to be 30% in 2100 geriatrics. In another study from Adana carried out on 501 geriatrics, Erkan et al. (12) reported the rate of anemia to be 32.5%. Both of these studies were carried out on patients aged 65 and over who had been referred to the internal medicine outpatient clinic so, it can be inferred that they had high rates of comorbidities and chronic diseases. Our study was carried out with 'community dwelling apparently healthy' geriatrics. There was no history of malignancies or chronic inflammatory diseases, except for COPD, among our participants. When these factors that

accompany aging were excluded, this high rate of anemia underlies the importance of studies in which anemia criteria and cut off levels have been questioned in special groups such as geriatrics (13,14).

Our study indicated that in geriatrics, cobalamin and folate deficiency were frequent and to identify the megaloblastic anemia we used increased MCV. However, especially in geriatrics, since mixed nutritional deficiencies and factors causing microcytic anemia often accompany cobalamin and folate deficiency, there might be patients who went unnoticed. In almost one out of every four patients, cobalamin was low and in 25% of cases there was iron deficiency along with cobalamin deficiency. Besides, anemia due to cobalamin or folate deficiency was not identified in geriatrics. As it has also been shown in the Leiden 85-Plus study, association of cobalamin or folate deficiency with anemia was poor, only severe deficiencies were related to anemia (15).

In the NHANES III study 34% of anemias were nutritional and the proportion of IDA was 20% in nutritional anemias (7). In our study there was iron deficiency in 22% of all geriatrics and IDA was the most common type of anemia, with a rate of 41%. Although in most anemics with iron deficiency the red cells were microcytic, almost one in five was normocytic. Mixed anemia that includes hypothyroidism and cobalamin deficiency, which is frequent in our population, may be the reason for that result. When patients are assessed in terms of iron deficiency, measuring ferritin levels to evaluate body iron store is a common approach. However, ferritin physiologically rises with age and there is a high occurance of inflammatory diseases in geriatrics (5,16). So, ferritin loses its importance in the diagnosis of IDA in this population, particularly for the values above 15 ng/dl. In fact, we found that the ferritin levels were similar in geriatric groups with and without iron deficiency.

In our study we found unexplained anemia to be 37%; although we did not use advanced examinations, this rate is much higher than expected for community dwelling people. In fact, the 'unexplained anemia' statement is not appropriate for this group. When advanced examinations are conducted, the potential factors responsible for anemia can be identified, and the truly unexplained, or senile or idiopathic anemias can be detected. For instance, although we did not note renin-angiotensin system inhibitors (RAS-I) as a drug which leads to anemia, 15 of geriatrics with unexplained anemia had been using RAS-I. Some studies have reported that RAS-I may lead to anemia via erythropoietin (17,18). Likewise, COPD may lead to anemia because it is an inflammatory disease (19). When other reasons are excluded with advanced examinations, this knowledge can be significant in determining unexplained anemias. Nevertheless, even in some studies carried out using advanced examinations such as bone morrow aspiration and hemoglobin electrophoresis, unexplained anemia was still high. For instance, in a recent study by Artz and Thirman (20) in 2011, 170 anemic geriatrics from hematology clinic were assessed and it was found that 43.7 % of anemias were unexplained anemias. In 2011 Price et al. (21) studied the etiology of anemia in geriatrics using advanced examinations; however, they could not identify 35% of the etiologies.

When trying to classify the anemias in terms of etiology, it must not be forgotten that plenty of cases are multifactorial. Fifteen of 56 geriatrics whom we considered IDA experienced at least stage-3 renal insufficiency, six of them had COPD associated with inflammation and two of them had manifest hypothyrodism (fT4<0.8 µg/dl). Since chronic inflammation and impaired iron absorbtion have a significant role in the pathogenesis of anemias associated with CKD, it is not possible to make clear distinctions between renal anemia and ACD. Therefore, the term 'dominant etiology' is more convenient for these conditions.

Limitations of the Study

The Melen study, whose data we used, was conducted to evaluate cardioprotective effects. For that reason, parameters such as peripheral blood smear, reticulocyte index, transferrin receptor index, homocysteine and bone morrow aspiration could not be examined. Therefore, it was not possible to distinguish the real idiopathic anemias.

In conclusion, this cross-sectional study demonstrates that anemia in the Turkish geriatric population may constitute a more frequent and major problem than expected. There have been very few studies on this issue in Turkey, and the present study is one of the significant ones conducted with community dwelling geriatrics. Finally, we would like to emphasise that anemia should not be considered as an outcome of ageing.

We would like to declare that there is not conflict of interest.

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