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Associations between anemia and dependence on basic and instrumental activities of daily living in older women

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Abstract

Aim The aim of the present study was to examine the relationship between anemia and basic and instrumental activities of daily living in older female patients.

Methods 540 older female outpatients were included in this cross-sectional study. Anemia was defined as a hemoglobin below 12 g/dL. Patients' demographic characteristics, comorbidities, Geriatric Depression Scale, Mini Nutritional Assessment, and Mini-Mental State Examination (MMSE) were also recorded. Handgrip strength (HGS) was measured with a hand dynamometer to detect dynapenia. Basic Activities of Daily Living (BADL) and Instrumental Activities of Daily Living (IADL) questionnaires were used to evaluate functional capacity.

Results The mean age of the participants was 77.42 ± 7.42 years. The prevalence of patients with anemia was 35%. A significant difference was observed between anemic and non-anemic groups in terms of age, presence of diabetes mellitus (DM), hypertension, coronary artery disease (CAD), chronic kidney disease (CKD), malnutrition, dynapenia, and MMSE, BADL and IADL scores ($p < 0.05$). In multivariate analysis, after adjustment for age, DM, hypertension, CAD and CKD; there were significant associations between anemia and reduced BADL/IADL scores, dynapenia, falls, the risk of falls, MMSE, and malnutrition ($p < 0.05$). After adjusting for all confounding variables, deterioration in total BADL and IADL total scores were still more common among anemic older females than those without anemia ($p < 0.05$).

Conclusion One out of every three older women presenting at one outpatient clinic were anemic. Anemia was observed to be associated with dependence in both BADL and IADL measures. Therefore, the presence of anemia in elderly women should be routinely checked, and possible causes should be investigated and treated to improve their functional capacity.

Keywords Anemia, Older, Activities of daily living, Dependence, Women

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Introduction

The frequency of anemia rises with increasing age, reaching a prevalence of 17% in older persons > 65 years [1]. Anemia, defined by the WHO as a hemoglobin (Hb) concentration of < 12 g/dl in women and < 13 g/dl in men, negatively impacts the health of the elderly population. However, Hb levels decline with age and may differ in different ethnic groups [2]. Causes of anemia in older adults include nutritional deficiency, chronic kidney disease, chronic inflammation, and occult blood loss from gastrointestinal disorders. Additionally, multiple underlying disorders have a higher prevalence among older adults, including, for example, myelodysplastic syndrome (MDS), other blood cell disorders, and cancer. In older adults, different etiologies may act synergistically contributing to the development of anemia [3, 4].

The overall prevalence of anemia in elderly individuals ranges from 10 to 24%. Older adults admitted to hospital are more likely to experience anemia (40%), and an even higher prevalence has been observed among (47%) nursing home residents [4]. Low Hb levels have been identified as a potentially important risk factor for cardiovascular diseases, cognitive impairment, insomnia, impaired mood, and restricted quality of life [5]. In addition, the presence of anemia is significantly associated with more frequent hospitalization and longer hospital stays [5]. Anemia has also been associated with geriatric syndromes in the elderly. In a study by Kara et al., anemia was found to be associated with frailty, polypharmacy, malnutrition, falls, and decreased muscle strength and therefore was concluded to be an indicator of general poor health in older women [6]. Moreover, insomnia and daytime sleepiness, which are important health problems known to impact quality of life in the elderly, were observed to be more frequent in patients with anemia [7]. Owing to these negative outcomes related to anemia, it is speculated that the Hb cut-offs determined several years ago for adult men and women should be targeted at higher values for the elderly [8].

The maintenance of independence in basic activities of daily living (ADLs) represents one of the major goals in geriatric care. Functional status has shown to be an important predictor of major health-related events, such as institutionalization and death [9, 10]. Functionality as applied to older adults may be defined as the capacity of one's cognitive and physical performance being sufficient to fulfill the activities of daily living independently [9]. An important focus of geriatric medicine is to implement comprehensive geriatric tests, to detect factors leading to negative outcomes and to provide possible treatment options [11]. Recently, anemia has been associated with loss of physical function, independent of the underlying disease status [9, 10]. Anemia reduces the oxygen-carrying capacity of the blood, which may lead to pathological changes that can cause fatigue, decreased exercise tolerance, and limitation of physical activity. Fatigue and dizziness can lead to falls. These symptoms may also be responsible for prolonged bed rest and limitation of physical activity [12, 13]. However, the number of studies investigating how anemia affects functional capacity in the elderly is limited, and the factors that may cause anemia and concurrently affect daily living activities have not been eliminated in these studies.

Given this background the aim of the present study was to evaluate the relationship between anemia and each of the ADLs while controlling for potentially important confounding variables. Moreover, only older females were included in the present study because of hormonal, socioeconomic and anthropometric differences between the sexes that may affect the development, of both anemia and geriatric syndromes/comprehensive geriatric assessment parameters.

Methods

Patients

A total of 540 patients who presented to a geriatric outpatient clinic in Turkey and underwent comprehensive geriatric assessment (CGA) between January 2021 and October 2023 were included in the cross-sectional study.

Inclusion/exclusion criteria

Patients aged greater than or equal to 65 years who attended an appointment at a geriatric outpatient clinic were included in the study. Male patients, those with acute bleeding (e.g., massive hematuria, hematochezia, melena, hematemesis, and intra-abdominal bleeding), moderate and severe dementia, those who could not participate in CGA owing to an existing condition (e.g. delirium), localized muscle strength reduction as a result of stroke, visual and/or hearing impairment preventing understanding of instructions during examination, those who did not want to participate, having a terminal disease (e.g. cancer), and had been hospitalized for a life-threatening illness or underwent major surgery in the last 6 months were not included in the study. After exclusion data were collected on a total of 540 patients whose data were included in the present study analysis (Fig. 1).

Main outcomes

Barthel Index for Activities of Daily Living (BADL) and Lawton Instrumental Activities of Daily Living (IADL) scale

The Barthel Index for Activities of Daily Living (BADL) records the level of independence and functional status in basic daily activities, including, eating, bathing, dressing, bowel/bladder control, toileting, transfers from bed to chair, mobility on flat surfaces, and stair climbing.

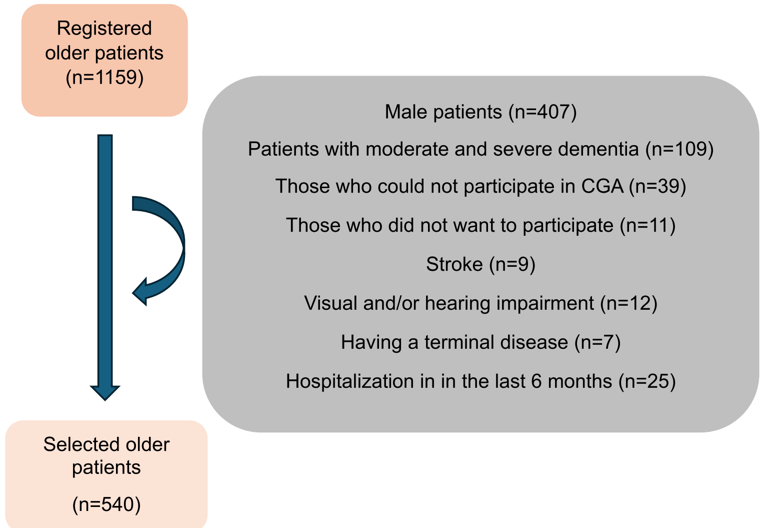

Fig. 1 Flowchat of the study

BADL is scored on a scale of 0 to 100 with 0 indicating dependency on another person and 100 indicating independence. The BADL is divided into five categories (100–91: fully independent; 99–91: mildly dependent; 62–90: moderately dependent; 61–21: highly dependent; 20–0: fully dependent) [14].

Disability levels in community-dwelling older adults were first evaluated by Lawton and Brody in 1969 who developed the Lawton Instrumental Activities of Daily Living Scale (IADL) to achieve this aim. The IADL is a commonly used assessment tool for this outcome among older adults. The IADL measures eight activities, including using a telephone, shopping, food preparation, housekeeping, laundry, use of transportation, responsibility for taking own medication, and ability to handle finances. On the Turkish version of the IADL each individual activity is scored on a scale from 0 to between 2 and 4. Low scores indicate a high degree of dependency, and the sum of scale runs from 0 to 23. The total score is interpreted as follows: 0–8: dependent; 9–16: semi-dependent; 17–23: independent [15].

Comprehensive geriatric assessment

The following patient information was collected and recorded: age, education level, and the following comorbidities: diabetes mellitus (DM), hypertension (HT), coronary artery disease (CAD), chronic kidney disease (CKD), chronic obstructive pulmonary disease, cerebrovascular disease, congestive heart failure, peripheral artery disease, Parkinson's Disease, and osteoarthritis. All participants completed the Mini-Mental State Examination (MMSE), Geriatric Depression Scale-15 for neurocognitive evaluation, Tinetti Performance-Oriented Assessment of Mobility (POMA) and Timed Up and Go Test (TUG), for mobility evaluation. Standardized MMSE was used to evalute cognitive function and the permission was obtained from the Molloy DW for the use of it [16]. Moreover, the Mini Nutritional Assessment (MNA) was carried out on all patients to record nutritional status. If the total MNA score was < 17, the patient was categorized as malnourished. Patients were considered as experiencing falls if they reported having fallen at least once in the previous year except for slipping on a carpet or on wet ground [9] and a POMA score less than 19 was categorized as having a high risk of falling. A score of greater than or equal to 5 on the GDS-15 was categorized as depression. Dynapenia was defined as having a grip strength less than 16 kg [17–21].

Laboratory findings

To record inflammatory markers, biochemical, metabolic, and nutritional status of patients' laboratory tests were performed. These tests consisted of complete blood count, kidney and liver functions, thyroid stimulating hormone, HbA1c and iron levels, iron-binding capacity (IBC), ferritin, vitamin B12, folic acid and vitamin D (25-hydroxy D3). Creatinine clearance from the kidney was calculated using the glomerular filtration rate (GFR) by employing the chronic Renal Disease Epidemiology Collaborative (CKD-EPI) equation. Chronic Kidney Disease (CKD) is defined as kidney damage or estimated GFR below 60 ml/min/1.73 m2.

The definition of anemia

Anemia was considered when the hemoglobin concentration was below 12 g/dL.

The study was aimed to investigate the relationship between anemia and BAD and IADL in older female patients.

Statistical analyses

Descriptive data from qualitative variables are presented as numbers and percentages, and as mean, standard deviation for quantitative variables. The conformity of the quantitative variables to the normal distribution was evaluated with the Kolmogorov Smirnov test. The Student t test was used to compare means of two independent groups. Pearson chi-square analysis was used for comparisons between the groups in terms of the ratios of the relevant qualitative variables. Logistic regression analysis was used to evaluate the relationships between the dependent variable and the independent variables. Enter method was used as variable selection method. The statistical significance level was taken as 0.05, and the SPSS (version 26) package program was used for analyses.

Results

Of 540 older female patients, 35.18% ($n=190$) had anemia. The mean age of the patients was 77.42 ± 7.42 years. Patient characteristics, comorbidities, laboratory findings and geriatric syndromes/CGA parameters are summarized in Table 1. A significant difference was observed between the anemic and non-anemic groups in terms of age, the presence of DM, HT, CAD and CKD ($p<0.05$). There was no difference between the two groups in terms of education and other comorbidities ($p>0.05$) (Table 1).

Numerous laboratory parameters differed between groups with and without anemia. While MCV, iron and GFR were lower in the group with anemia, red cell distribution width and IBC were higher. All CGA parameters were more negatively affected, except for geriatric depression scale score and MMSE, geriatric syndromes were more common in patients with anemia compared to those without anemia (Table 1).

Table 2 shows that after adjusting for age, in those with anemia compared to those without anemia, adverse effects on malnutrition, dynapenia, BADL, IADL, falls, the risk of falls and MMSE scores were statistically significant ($p<0.05$) (Model 2). In the Model 3 multivariate analysis, adjustment was made according to age, DM, HT, CAD, and CKD. BADL [OR: 0.98 (95% CI 0.96–0.99)], IADL [OR: 0.95 (95% CI: 0.91–0.98)], dynapenia [OR: 1.62 (95% CI: 1.08–2.44)], falls (OR: 2.16 (95% CI: 1.45–3.21)], the risk of falls (OR: 1.87 (95% CI: 1.15–3.04)], MMSE [OR: 0.91 (95% CI: 0.84–0.99)] and malnutrition [OR: 1.86 (95% CI: 1.08–3.19)] scores were statistically significant ($p<0.05$). In Model 4, in addition to the confounders in Model 3, MMSE and malnutrition were added to the adjustment, and the significant association of anemia with falls, the risk of falls deterioration in BADL and IADL scores remained ($p<0.05$) (see Table 2).

Table 3 shows that after adjusting for age, DM, HT, CAD and CKD, in those with anemia compared to those without anemia, adverse effects on feeding [OR: 2.74 (95% CI: 1.18–6.36)], bathing [OR: 1.34 (95% CI: 1.01–1.76)], dressing [OR: 1.57 (95% CI: 1.02–2.42)], mobility [OR: 0.95 (95% CI: 0.91–0.98)], and stair climbing [OR: 1.49 (95% CI: 1.13–1.97)], scores were statistically significant ($p<0.05$) (Model 1). In Model 2, in addition to the confounders in Model 1, MMSE and malnutrition were added to the adjustment, and the significant associations were observed between anemia with mobility [OR: 1.84 (95% CI: 1.28–2.64)], and stair climbing [OR: 1.36 (95% CI: 1.02–1.81)] ($p<0.05$). In Model 3, in addition to the confounders in Model 2, dynapenia was added to the adjustment, and the significant association of anemia with stair climbing remained ($p<0.05$) (see Table 3).

Table 4 shows that after adjusting for age, DM, HT, CAD and CKD, in those with anemia compared to those with no anemia, adverse effects on shopping [OR: 1.23 (95% CI: 1.02–1.43)], food preparation [OR: 1.29 (95% CI: 1.08–1.53)], housekeeping [OR: 1.61 (95% CI: 1.08–2.41)] and mode of transportation [OR: 1.31 (95% CI: 1.10–1.55)] scores were statistically significant ($p<0.05$) (Model 1). In Model 2, in addition to the confounders in Model 1, MMSE and malnutrition were added to the adjustment, and the significant association of anemia with shopping [OR: 1.18 (95% CI: 1.00–1.38)], food preparation [OR: 1.22 (95% CI: 1.02–1.46)] and mode of transportation [OR: 1.25 (95% CI: 1.05–1.49)] remained. In Model 3, in addition to the confounders in Model 2, dynapenia was added to the adjustment, and the significant association of anemia with food preparation and mode of transportation ($p<0.05$) remained (see Table 4).

Figure 2 shows the casual diagram showing the confounders and the association between anemia and dependence of BADL and IADL.

Discussion

This study investigated the relationship between anemia and basic and instrumental activities of daily living in older female patients. The frequency of DM, HT, CAD, and CKD was higher in those with anemia than those without anemia. Among geriatric syndromes, depression, malnutrition, dynapenia, and cognitive impairment were more common in anemic patients. Dependence on ADLs was higher in older women with anemia than in those without. Moreover, this significant difference persisted after adjusted for the geriatric syndromes that could affect this dependence [10, 22].

Table 1 Patients's characteristics according to anemic and non-anemic groups

	Older female		
	Anemia (-) *n* = 350	**Anemia (+) *n* = 190**	**p**
Age, years	76.3 ± 7.7	79.5 ± 7.3	< 0.001
Education, years	4.6 ± 4.3	4.2 ± 4	0.178
Comorbidities (%)			
Diabetes mellitus	33.4	42.6	0.034
Hypertension	70.5	81.6	0.005
Coronary arterial disease	13	21.2	0.013
Chronic obstructive pulmonary disease	4.3	7.4	0.131
Cerebrovascular disease	6.9	10	0.205
Congestive heart failure	8	11.6	0.171
Pulmonary arterial hypertension	2	1.1	0.407
Parkinson disease	4	6.3	0.236
Osteoarthritis	23.1	24.2	0.762
Chronic kidney disease	29.4	54.3	< 0.001
Laboratory analyses (Blood)			
Hemoglobin (Hb-g/dl)	13.2 ± 0.8	10.7 ± 1	< 0.001
Hematocrit (Hct-%)	40.9 ± 2.9	33.9 ± 3	< 0.001
Mean Corpuscular Volume (MCV-fL)	88.8 ± 4.6	85.6 ± 7.6	< 0.001
Red Cell Distribution Width (RDW- %)	13 ± 1.3	14.1 ± 2.2	< 0.001
White Blood Cell (WBC-mm^3)	7.7 ± 2.1	7.8 ± 3.5	0.501
Platelet (PLT- mm^3)	256.1 ± 66.6	263.4 ± 77.7	0.252
Mean platelet volüme (MPV-fl)	8.4 ± 1.7	8.2 ± 1.8	0.161
Iron (Fe-mcg/dL)	75.2 ± 27.3	50.8 ± 26.6	< 0.001
Iron Binding Capacity (IBC-mcg/dL)	240.3 ± 63.2	260 ± 86.4	0.050
Ferritin (ng/mL)	68.1 ± 81.7	82.3 ± 109.1	0.580
Vitamin B12 (pg/mL)	501.3 ± 379.7	540.2 ± 389.9	0.180
Folate (ng/mL)	8.1 ± 3.8	7.6 ± 4	0.103
Creatinine Clearence (CrCl-ml/min)	68.3 ± 15.4	58.1 ± 17	< 0.001
25-OH-D3 (VitD-ng/mL)	25.4 ± 15.9	26.7 ± 16	0.257
Tyroid Stimulating Hormone (mU/L)	2 ± 2.3	1.6 ± 1.6	0.251
Free T4	7.7 ± 6.5	7.4 ± 6.8	0.775
Glucose(mg/dl)	119 ± 49	121.4 ± 47.6	0.966
C-reactive Protein (CRP- mg/L)	9 ± 22.9	12 ± 21.6	0.058
LDL-C (mmol/L)	143.7 ± 42.8	124.7 ± 34	< 0.001
Triglycerides (mmol/L)	154.6 ± 84.3	144.4 ± 141.4	0.064
HDL-C (mmol/L)	56 ± 14.4	54.2 ± 15.8	0.189
Comprehensive geriatric assessment/geriatric syndromes			
MNA score	23 ± 4.5	21.1 ± 4.8	< 0.001
Calf circumference (cm)	36.7 4.8	36.1 4.5	0.219
Mid-arm circumference (cm)	29.8 4.3	28.9 4.1	0.006
GDS-15	5.3 ± 4.3	5.6 ± 3.8	0.150
Hand grip strength (kg)	17.3 ± 6.2	15 ± 5.1	< 0.001
MMSE	25.9 ± 2.5	25.2 ± 2.3	0.003
SARC-F score	3.1 ± 2.9	4.6 ± 3	< 0.001
Falls, number	0.8 ± 1.9	1.6 ± 2.8	< 0.001
POMA scores	13.7 ± 3.7	12.1 ± 4.5	< 0.001

MNA Mini Nutritional Assessment (0 [worst]-30 [best]), *GDS-15* Geriatric Depression Scale-15 (0 [best]-15 [worst]), *MMSE* Mini-Mental State Examination (0 [worst]-30 [best]), *BADL* Basic activities of daily living (0 [worst]-100 [best]), *IADL*: Instrumental activities of daily living (0 [worst]-23 [best]), *POMA* Tinetti performance oriented mobility assessment (0 [worst]-28 [best])

Table 2 Multiple logistic regression analysis of the relationship between geriatric assessment parameters/geriatric syndromes and anemia

	Model 1		Model 2		Model 3		Model 4	
	OR	**P**	**OR**	**P**	**OR**	**P**	**OR**	**p**
Age	1.06 (1.03–1.08)	< 0.001	-	-	-	-	-	-
DM	1.48 (1.03–2.12)	0.034	1.73(1.18–2.54	0.005	-	-	-	-
HT	1.85 (1.20–2.86)	0.005	1.59(1.02–2.48	0.040	-	-	-	-
CAD	1.80 (1.13–2.88)	0.014	1.64(1.02–1.65	0.041	-	-	-	-
CKD	2.85 (1.95–4.17	< 0.001	2.33(1.56–3.48)	< 0.001	-	-	-	-
Malnutrition	1.82 (1.13–3.03)	0.014	1.67(1.01–2.77)	0.045	1.86 (1.08–3.19)	0.024	-	-
Dynapenia	2.21 (1.54–3.18)	< 0.001	1.79(1.22–2.62)	0.003	1.62 (1.08–2.44)	0.019	-	-
Falls	2.44 (1.76–3.66)	< 0.001	2.36(1.63–3.43)	< 0.001	2.16 (1.45–3.21)	< 0.001	2.14 (1.43–3.20)	< 0.001
The risk of falls	2.40(1.6–3.68)	< 0.01	1.84(1.17–2.91)	0.008	1.87 (1.15–3.04)	0.011	1.71 (1.05–2.80)	0.031
MMSE	0.90 (0.84–0.97)	0.005	0.92(0.85–0.99)	0.027	0.91 (0.84–0.99)	0.037	-	-
BADL score	0.970(0.95–0.98)	< 0.01	0.97(0.96–0.99)	< 0.001	0.98 (0.96–0.99)	0.03	0.98 (0.97-.99)	0.014
IADL score	0.92 (0.89–0.95)	< 0.01	0.94(0.91-.97	< 0.001	0.95 (0.91–0.98	0.003	0.96 (092–0.99)	0.035

OR Odds ratio, *DM* Diabetes Mellitus, *HT* Hypertension, *CAD* Coronary Arterial Disease, *CKD* Chronic Kidney Disease, *MMSE* Mini-Mental State Examination, *BADL* Basic Activities of Daily Living, *IADL* Instrumental Activities of Daily Living

Table 3 The Barthel activities of daily living results

	Model 1		Model 2		Model 3	
	Odd Ratio	**P**	**Odd Ratio**	**P**	**Odd Ratio**	**P**
Feeding	2.74 (1.18–6.36)	0.019	-	-	-	-
Bathing	1.34 (1.01–1.76)	0.038	-	-	-	-
Dressing	1.57 (1.02–2.42)	0.039	-	-	-	-
Toilet use	-	-	-	-	-	-
Stairs	1.99 (1.40–2.84)	< 0.001	1.84 (1.28–2.64)	0.001	1.79 (1.24–2.60)	0.002
Bowel continence	-	-	-	-	-	-
Bladder continence	-	-	-	-	-	-
Transfer	-	-	-	-	-	-
Mobility	1.49 (1.13–1.97)	0.005	1.36 (1.02–1.81)	0.035	-	-
Grooming	-	-	-	-	-	-

Table 4 Lawton instrumental activities of daily living results

	Model 1		Model 2		Model 3	
	Odd Ratio	**P**	**Odd Ratio**	**P**	**Odd Ratio**	**P**
Ability to use telephone	-	-	-	-	-	-
Shopping	1.23 (1.025–1.43)	0.008	1.18 (1.00–1.38)	0.045	-	-
Food preparation	1.29 (1.08–1.53)	0.004	1.22 (1.02–1.46)	0.026	1.20 (1.00–1.44)	0.045
Housekeeping	1.61 (1.08–2.41)	0.018	-	-	-	-
Laundry	-	-	-	-	-	-
mode of transportation	1.31 (1.10–1.55)	0.002	1.25 (1.05–1.49)	0.013	1.20 (1.00–1.44)	0.047
Responsibility for own medications	-	-	-	-	-	-
Ability to handle finances	-	-	-	-	-	-

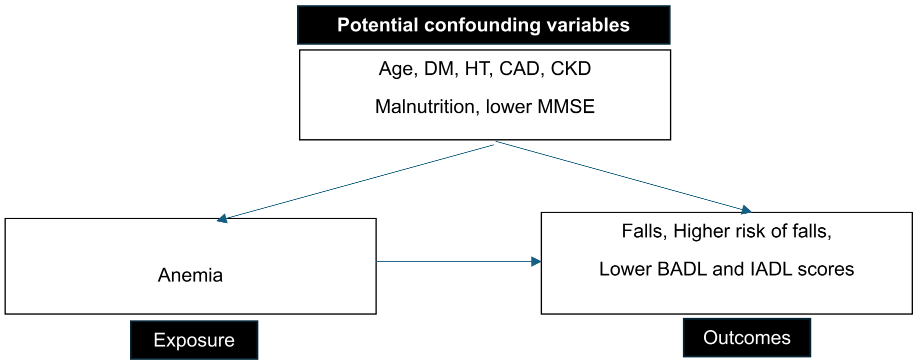

Fig. 2 The casual diagram showing the association between anemia and activities of daily living. Abbreviations: BADL: Basic activities of daily living; CAD: Coronary Arterial Disease; CKD: Chronic Kidney Disease; DM: Diabetes Mellitus; HT: Hypertension; IADL: Instrumental activities of daily living; MMSE: Mini-Mental State Examination

Anemia in older adults is multifactorial and is often caused by suppression of erythropoiesis due to chronic inflammation (infection, malignancy, inflammatory diseases, etc.) and nutritional deficiencies (iron, vitamin B12, and folate) [23]. However, despite all investigations, the cause of anemia cannot be determined in approximately 14% to 50% of older adults [23, 24]. In the current study, we observed anemia (Hb level below 12 g/dl) in 190 (35%) of 540 patients. This prevalence value, independent of the etiology, is higher than the prevalence data obtained from other studies [25]. For example, Stauder et al. showed the prevalence of anemia to be 10.2% in older women [4]. In another study, Semba et al. found that the prevalence of anemia was 21.4% in older women [26]. This may be related to the higher mean age of our patient group, as well as race, ethnicity, and comorbid diseases. On the other hand, Sahin et al. showed the prevalence of anemia was 58.3% in nursing homes among older women [27]. This rate is higher than the finding in the present study, which may be explained by lower functional capacities of patients in nursing homes or more common accompanying comorbid diseases and geriatric syndromes such as malnutrition that is a leading cause of anemia. Indeed, in their review, Beghe et al. revealed that the prevalence of anemia among older women ranges between 3.3% to 41% [28]. This variability may be related to several factors, including the study setting, the health status of the population in question, and the criteria used to define anemia.

In our study, anemia in older women was found to be associated with DM, HT, CAD, and CKD. Indeed, DM and anemia are common conditions in older adults, and have been found to be associated with an increased level of severity of multiple comorbidities (e.g., cardiovascular diseases) as well as an increase in risk of mortality [29]. Overtime DM may lead to micro and macrovascular damage, which may have an adverse impact on the circulatory system, nervous system, kidneys, and eyes. Anemia is known to increase these complications in older diabetic patients [29]. In a study of 981 patients, Michalak et al. found the rate of patients with a diagnosis of DM to be 24.9%. In the same study, among 145 older women, 20% of patients had both anemia and DM [29]. In our study, the rate of patients with anemia and DM was calculated to be 42.6%. Differences in the frequency of coexistence of anemia and DM may be due to several factors. Current literature suggests that the coexistence of anemia and DM is commonly observed in patients who are hospitalized or under the care of specialized clinics. The level of health care, age (as the prevalence of anemia and DM increases with age), the economic situation of the country in which the study was conducted, and the geographical location (altitude) are also of importance. The etiology of anemia in DM may be owing to several key factors, including chronic inflammation, nutritional deficiencies, concomitant autoimmune diseases, concurrent HT medication (particularly, angiotensin II receptor blockers) and antihyperglycemic agents (notably, metformin), hormonal changes, and kidney disease [30, 31]. In the presence of CKD, erythropoietin production is impaired and severe hypoproliferative anemia dominates the hematologic picture [32]. In turn, anemia can lead to CKD progression, increased mortality and decreased quality of life. Since CKD is associated with geriatric syndromes that may negatively affect ADLs in older adults, we adjusted for its effect in our study [33]. The same may also be true for anemia and cardiovascular disease. Culleton et al. demonstrated the association between anemia and cardiovascular risk. According to this study, the risk of CAD, HT and congestive heart failure is 3 to 4 times higher in the older patients with anemia [34]. Therefore, simultaneous treatment of anemia may be an important element in the management of these diseases.

In our study, we found that the dependence in both basic and instrumental life activities is more common in older women with anemia. This finding is consistent with previous studies. For example, Penninx et al. found that anemia was associated with disability and decreased physical performance in older adults [10]. Moreover, similar to the present study, this study showed that muscle strength is decreased in patients with anemia. However, in this study, the effect of dynapenia (decreased muscle strength) on ADLs was not eliminated, and malnutrition was not evaluated as an etiological factor of anemia [10]. Jia et al. found that anemia was significantly associated with ADLs in older Chinese females [35]. In this study, only the relationship between basic activities of daily living and anemia was examined, whereas the present study demonstrates that instrumental activities are also negatively affected by anemia. These findings suggest that lower Hb levels are associated with greater daily living activity dependence. This relationship can be associated with several possible underlying mechanisms. The impact of anemia on function and strength decline may be related to reduced muscle oxygenation [36]. Anemia-induced hypoxia is a crucial factor for cellular functions in all organs, particularly the brain and skeletal muscles, and this can result in any component of frailty, such as fatigue, weakness, depression, and impaired physical activity [22, 37, 38].

Dynapenia is an important factor altering the functional capacity of the elderly and causing disability [39]. Importantly, in a study with 10-years of follow-up anemia with dynapenia was associated with higher all-cause mortality risk, independent of socioeconomic factors, health behaviors and comorbidities [40]. An association between low Hb levels and low muscle strength has previously been observed in cross-sectional studies [40]. Alexandre et al., found that anemia was associated with dynapenia in 1168 older Brazilian adults [41]. Cesari et al., in a sample of 909 older adults residing in Italy, found that those with anemia presented a weaker ankle extension strength compared to those without anemia [42]. Additionally, a recent study reported that anemia was associated with dynapenia in older women, but not in older men [22]. Decreased oxygen delivery due to low Hb levels results in chronic hypoxia. Indeed, it is possible that chronic hypoxia may damage the musculoskeletal system, reducing muscle strength and thus leading to dynapenia. In addition, anemia associated fatigue may also lead to dynapenia, as fatigue is associated with low levels of physical activity and thus muscle disuse [43, 44]. All the above-mentioned findings relating to the impact of anemia on functionality show that it has a clear contribution to dynapenia. However, interestingly, we found that dependence in ADL (especially food preparation, climbing stairs, and transportation) was more common in older women with anemia, even after the confounding effect of dynapenia was adjusted for. This suggests that anemia may affect functionality not only through decreased muscle strength, but also through other mechanisms (eg, orthostatic hypotension or cerebral hypoperfusion).

There is also a close relationship between anemia, malnutrition and functionality. Ramel et al. demonstrated that anemia was correlated with biological (albumin, prealbumin, and lymphocyte count) and clinical (body mass index, weight loss, triceps skinfold thickness, mid-arm muscle circumference) parameters of malnutrition [45]. In our study, the prevalence of malnutrition was greater in patients with anemia. Particularly, the relationship between malnutrition and shopping and food preparation suggests that nutritional problems in the elderly may cause anemia. Moreover, our findings related to stair climbing in BADL and limitations in mobility and difficulties in transportation in IADLs, which may be associated with malnutrition sarcopenia [46]. Therefore, it is important to control for nutritional factors when assessing functionality. Another limitation may be that we did not evaluate the drug types, such as bone-marrow suppressing agents (e.g. methotrexate, metamizole) or antiplatelet/anticoagulant therapies. A clear strength of the present study includes the adequate sample size of patients with anemia. Moreover, it is advantageous that anemia screening and comprehensive geriatric evaluation were performed on the same day. A final strength is that only older women were included in the study; thus, sex-related effects were eliminated. Several limitations of this study should be considered. Firstly, those with anemia were not grouped according to the severity of the condition and were evaluated on a single outpatient visit. Second, erythropoietin levels were not routinely checked in all patients, which is important in deciding whether the anemia is transient or permanent. Another limitation of the study is that functional iron deficiency (transferrin saturation < 20%, ferritin > 100 ng/ml) was not examined in detail. Finally, the study utilized a cross-sectional design and thus direction of associations cannot be established. Anemia is likely to be an independent factor for these outcomes in our study, but it cannot be stated as the "cause."

In conclusion, one out of every three older women presenting to a Turkish outpatient clinic had anemia. Anemic women were older and had a higher incidence of DM, HT, CAD and CKD as comorbid diseases. Anemia is associated with dependence in both basic and instrumental activities of daily living. Particularly, cognitive dysfunction, dynapenia and malnutrition contribute to this association. However, anemia is associated with decreased functionality and increased falls, which is independent of all these factors. Therefore, older women should routinely be tested for anemia, and possible crosss should be investigated and treated to prevent these negative outcomes.

Abbreviations

BADL	Basic activities of daily living
CAD	Coronary Arterial Disease
CKD	Chronic Kidney Disease
DM	Diabetes Mellitus
HT	Hypertension
IADL	Instrumental activities of daily living
MMSE	Mini-Mental State Examination

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Availability of data and materials
The datasets used and analyzed during the current study will be made available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
Ethics approval was given by Bezmialem Vakif University Ethics Committee. All participants provided informed consent and all procedures have been performed in accordance with the Declaration of Helsinki.

Consent for publication
Not applicable.

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