

Association of anemia with comorbidity and polypharmacy in adults aged ≥ 80 years: an outpatient-based cross-sectional study

Seyit Burak Şam¹, Ayfer Durak²

¹Department of Family Medicine, Amasya University Sabuncuoğlu Şerefeddin Training and Research Hospital, Amasya, Türkiye

²Division of Geriatrics, Department of Internal Medicine, Amasya University Sabuncuoğlu Şerefeddin Training and Research Hospital, Amasya, Türkiye

ABSTRACT

Background: Anemia, multiple chronic conditions, and polypharmacy are common in older adults and are associated with adverse clinical outcomes. This study aimed to examine the relationship between anemia, chronic disease burden, and polypharmacy in individuals aged 80 years and older.

Methods: This single-center cross-sectional study included individuals aged ≥ 80 years who were followed in a Healthy Aging outpatient clinic. Anemia was defined using World Health Organization criteria. Comorbidity burden (≥ 4 chronic conditions) and polypharmacy (≥ 6 medications) were recorded. Multivariable logistic regression was used to identify factors independently associated with anemia.

Results: The study included 134 individuals. The mean age of the participants was 85.5 ± 3.9 years, and 61.2% were women. The overall prevalence of anemia was 51.5%. Compared to non-anemic individuals, those with anemia were older and had significantly higher comorbidity burden and a greater prevalence of polypharmacy. Hemoglobin levels were negatively correlated with both the number of medications and the number of comorbidities. In multivariable logistic regression analyses, age and polypharmacy were independently associated with anemia in one model. In an alternative model accounting for collinearity, age and comorbidity burden remained independently associated with anemia.

Conclusions: Anemia is highly prevalent among individuals aged ≥ 80 years and is associated with comorbidity burden and polypharmacy. The findings suggest that a more holistic clinical approach that also considers these factors may be useful in the evaluation of anemia in this age group. Prospective studies are needed to clarify the direction of these associations.

Keywords: Anemia, aged, 80 and over, comorbidity, multimorbidity, polypharmacy

Introduction

Anemia is a health problem that is frequently observed in the older age group and is important in terms of clinical outcomes. The World Health

Organization (WHO) defines anemia as a hemoglobin level of <13 g/dL in men and <12 g/dL in women.^[1] While the prevalence of anemia in community-dwelling older adults ranges from 8.1% to 24.7%, this rate increases to 31–60% in

nursing homes and up to 40–72% in hospitalized older adults.^[2]

In older individuals, anemia is evaluated not only as a hematological disorder, but as a multidimensional clinical condition associated with falls, reduced functional capacity, cognitive impairment, and increased mortality. Therefore, the early recognition and appropriate management of anemia in the older age group is of importance in terms of preserving functionality and maintaining quality of life.^[2] However, anemia in advanced age often appears not as a condition attributable to a single cause, but rather as a complex picture in which multiple clinical factors coexist. With aging, a decrease in physiological reserve, an increase in chronic disease burden, inflammatory processes, nutritional deficiencies, and malignancies may contribute to the development of anemia.^[3]

In this context, individuals aged eighty years and older represent a distinct population characterized by increased comorbidity burden, polypharmacy, and heterogeneous clinical features. The prevalence of comorbidities and multiple medication use both makes clinical decision-making processes more difficult and complicates the interpretation of laboratory abnormalities such as anemia.^[4]

On the other hand, polypharmacy is evaluated not only as multiple medication use, but also as an indicator reflecting an individual's overall health status and disease burden.^[5] In the literature, there are findings indicating that multiple medication use may be related to anemia through mechanisms such as gastrointestinal bleeding, disorders of nutrient absorption, and chronic inflammation.^[2] However, it is thought that approaches aimed at reducing polypharmacy (deprescribing) in older adults may contribute to the reduction of medication-related adverse effects.^[6]

However, studies evaluating the relationships between anemia, comorbidity burden, and polypharmacy in older adults are limited in our country. Although the general definition of the elderly population typically includes those aged 65 and over, this study focused specifically on individuals aged 80 years and older. This selection was primarily determined by the specific setting of our study, the 'Healthy Aging Outpatient Clinic,' which exclusively provides care for this age group. Furthermore, individuals aged 80 years and older represent a distinct population characterized by increased comorbidity burden and polypharmacy compared to younger older adults. This study aims to evaluate the relationship between anemia and factors such as comorbidity burden and polypharmacy in adults aged 80 and over. By using real-world clinical data, this study aims to provide findings that are relevant and practical for primary care settings. We hypothesized that anemia would be associated with a higher comorbidity burden and polypharmacy in this age group.

Material and Methods

Study design and ethical approval

This single-center, cross-sectional study was conducted in Amasya University Sabuncuoğlu Şerefeddin Training and Research Hospital between May and November 2025. In this province, follow-up of adults aged ≥80 years within the Ministry of Health 'Healthy Aging' program is centralized in this unit; therefore, the sampling frame was inherently single-center. The source population consisted of individuals aged 80 years and older who were registered and followed in the Healthy Aging Outpatient Clinic/Program. Participants were assessed either during outpatient visits or home visits. Data for each participant were collected only once at the time of assessment by a Family Medicine Specialist with over five years of experience in geriatric care and a registered nurse with at least ten years of

experience in home care services. Both researchers had received training on the administration of the assessment forms within the scope of the Healthy Aging Program to ensure standardization. This standardized protocol comprised a systematic three-step workflow: First, a face-to-face interview was conducted to administer the geriatric assessment scales. Second, the patient's self-reported chronic diseases and medication list were cross-referenced with the national electronic health record system and hospital database to ensure accuracy and minimize recall bias. Finally, venous blood sampling was performed. Regardless of the assessment setting, the same data collection method was applied to all participants.

The study was conducted in accordance with the ethical principles of the Declaration of Helsinki and was approved by the local ethics committee (Date: 28.04.2025; Approval No: E-76988455-050.04-258208). Written informed consent was obtained from all participants or their legal representatives prior to data collection. Because all clinical and laboratory assessments were performed as part of this routine medical care, the study incurred no additional costs and received no specific funding.

Participants and inclusion criteria

Consecutive enrollment was employed to help reduce investigator-driven selection bias.

This approach was aligned with the structure of the Ministry of Health's 2024 "Healthy Aging Program," in which individuals aged 80 years and older are followed at this center.

All eligible individuals registered in the program were consecutively included in the study, irrespective of the assessment setting. Individuals with the following characteristics were excluded:

- Evidence of acute infection (fever, clinical/objective signs of infection, a documented diagnosis in the medical record, or antibiotic treatment),

- Malignancy cases receiving active chemotherapy,
- Individuals with active clinical bleeding.

For participants who could not be directly assessed due to cognitive impairment, sensory disability, or communication difficulties, data were obtained from primary caregivers.

Sample size

Sample size was determined based on the principle that logistic regression analysis requires at least 10 events per variable ($EPV \geq 10$) for each independent variable.^[7] Among the 134 participants included, anemia was identified in 69 individuals, meeting the minimum number of events required for analysis in a five-variable model. Thus, the sample size was considered adequate for multivariable logistic regression analysis.

Variables and measurement methods

Demographic data

Demographic characteristics such as age, sex, and living alone status were recorded.

Comorbidity assessment

Common chronic diseases were queried and recorded according to International Classification of Diseases (ICD-10) codes. These included hypertension, diabetes, heart failure, dementia, chronic obstructive pulmonary disease (COPD), cerebrovascular disease, malignant neoplasms (cancer), and Parkinson's disease. The total number of chronic diseases for each participant was calculated and used in analyses both as a continuous variable and as a categorical variable (≥ 4 comorbidities: high comorbidity burden). Because the presence of four or more comorbidities is considered a threshold reflecting clinical frailty in older adults in the literature, this classification was also adopted in the present study.^[4,8,9]

Medication use and polypharmacy assessment

Medications used by participants were grouped according to the Anatomical Therapeutic Chemical (ATC) classification system. The most frequently used medication groups included analgesics (paracetamol, non-steroidal anti-inflammatory drugs, opioids), central nervous system-related drugs (antidepressants, antipsychotics), gastric acid suppressants, and laxatives.

In addition, the total number of medications for each participant was recorded. While polypharmacy is commonly defined as the use of ≥ 5 medications, definitions in the literature vary significantly depending on the population studied.^[10] In our cohort of 'oldest-old' adults, the median number of prescribed medications was found to be 5.5. Therefore, to avoid a ceiling effect and to better stratify the high medication burden in this specific age group, a higher threshold of ≥ 6 medications was adopted for this study.

Functional status

Functional status was assessed using the Katz Index of Activities of Daily Living (ADL). This index consists of six domains—bathing, dressing, toileting, transfer (bed–chair), continence, and feeding—and is scored from 0 to 6. A score of 0 indicates total dependence, while a score of 6 indicates full independence. Participants who were unable to perform at least one of these activities were classified as dependent.^[11]

Nutritional status

Nutritional status was assessed using the Mini Nutritional Assessment–Short Form (MNA-SF). Scores of ≤ 7 indicated malnutrition, 8–11 indicated risk of malnutrition, and ≥ 12 indicated normal nutritional status. In analyses, malnutrition and risk of malnutrition groups were combined and classified as “presence of malnutrition.” Participants receiving oral nutritional supplements were also included in this group.^[12]

Assessment of depressive symptoms

Depressive symptoms were assessed using the Geriatric Depression Scale (GDS-30). A score of ≥ 11 was accepted as indicating the presence of a depressive state.^[13]

Definition and grouping of anemia

To ensure international comparability, WHO-recommended hemoglobin thresholds were used. Accordingly, individuals with hemoglobin (Hb) levels < 13.0 g/dL in men and < 12.0 g/dL in women were considered anemic. Participants were divided into two groups (anemia present vs. absent) according to these criteria.^[1]

Laboratory measurements

Venous blood samples were obtained either in the hospital setting or during home visits. Samples were collected in accordance with biosafety rules, with precautions taken to minimize hemolysis risk, and were transported to the laboratory on the same day under 2–8°C conditions.

Complete blood count, hemoglobin (g/dL), and mean corpuscular volume (MCV, fL) measurements were performed using a fully automated hematology analyzer (Sysmex XN-1000, Japan). Serum iron ($\mu\text{g/dL}$), ferritin (ng/mL), vitamin B12 (pg/mL), folate (ng/mL), TSH ($\mu\text{IU/mL}$), and 25-OH vitamin D (ng/mL) levels were measured using chemiluminescent immunoassay (CLIA) (Siemens Advia Centaur XP, USA). Glucose (mg/dL), urea (mg/dL), creatinine (mg/dL), uric acid (mg/dL), albumin (g/L), and CRP (mg/L) were analyzed using appropriate enzymatic and colorimetric methods (Beckman AU 5800, USA).

Statistical analysis

Analyses were performed using IBM SPSS Statistics (version 27.0; IBM Corp., Armonk, NY, USA). The distribution of continuous variables was assessed using the Kolmogorov–Smirnov test. Normally distributed data were presented

as mean $\pm$ standard deviation, and non-normally distributed data as median (minimum–maximum). Categorical variables were presented as number and percentage (%). To compare differences between groups according to anemia status, the chi-square test was used for categorical variables, and the independent samples t-test or Mann–Whitney U test was applied for continuous variables depending on distribution.

Multivariable logistic regression analysis was performed to identify independent factors associated with anemia. Candidate covariates were selected based on both statistical and clinical considerations. First, variables showing an association with anemia in univariable analyses at a significance level of $p < 0.05$ were considered eligible. Second, variables known from previous literature to be clinically relevant to anemia in older adults (age, sex, nutritional status, renal function, polypharmacy, and comorbidity burden) were also included, regardless of their univariable significance. Accordingly, the following variables were evaluated in the multivariable models: age, sex, malnutrition, urea level, polypharmacy, and comorbidity burden. Because a strong correlation was observed between the number of medications and the number of comorbidities ($r = 0.765$), indicating potential multicollinearity, these variables were not entered simultaneously into the same model. Instead, two separate multivariable models were constructed: model 1 included polypharmacy, and model 2 included comorbidity count. Variable selection was performed using the Forward Likelihood Ratio (Forward LR) method. Model fit was assessed using the Hosmer–Lemeshow goodness-of-fit test. Odds ratios (ORs) with 95% confidence intervals (CIs) were calculated to estimate the strength of associations. Logistic regression assumptions and

interpretation of ORs were based on established methodological approaches.^[14] As there were no missing data, no imputation method was applied. Statistical significance was defined as $p < 0.05$ for all analyses.

Results

Descriptive characteristics

A total of 134 participants were included in the study. The mean age of the participants was 85.5 ± 3.9 years, and 61.2% were women. Of the individuals, 23.9% were living alone, and 48.5% were dependent in activities of daily living. The overall prevalence of anemia was found to be 51.5%. When the distribution by sex was examined, the prevalence of anemia was determined to be 52.4% in women and 50.0% in men. Hypertension (82.8%) was the most frequently reported chronic disease. High comorbidity burden (≥ 4 comorbidities) was present in 56.7% of participants, and polypharmacy (≥ 6 medications) was observed in 50.0%. The most commonly used medication groups were analgesics (67.1%) and proton pump inhibitors (47.0%) (Table 1).

Clinical and laboratory characteristics according to anemia status

In comparisons by anemia status, participants in the anemia group had a significantly higher mean age ($p = 0.048$). High comorbidity burden (69.6% vs. 43.1%; $p = 0.002$), comorbidity count (median: 4 vs. 3; $p = 0.008$), and use of ≥ 6 medications (63.8% vs. 35.4%; $p = 0.001$) were also significantly more frequent in the anemia group. When laboratory findings were examined, hemoglobin and iron levels were significantly lower in the anemia group, whereas urea levels were higher ($p < 0.01$; $p = 0.008$; $p = 0.019$, respectively) (Table 2).

Table 1. Descriptive characteristics of the study population.

Sample size (n=134)	Mean±SD	Median (min-max)
Age (years)	85,54±3,877	-
Gender n(%)		
Female	82 (61.2)	-
Male	52 (38.8)	-
n (%)		
Alone (Living Status)	32 (23.9)	-
Dependency (ADL)	65 (48.5)	-
Malnutrition (MNA-SF)	27 (20.1)	-
Depressive Symptoms (GDS)	59 (44.0)	-
Comorbid disease n (%)		
Hypertension	111 (82.8)	-
Dementia	42 (31.3)	-
Diabetes Mellitus	35 (26.1)	-
Congestive Heart Failure	25 (18.7)	-
Chronic Obstructive Pulmonary Disease	18 (13.4)	-
Parkinson's Disease	12 (9.0)	-
Cerebrovascular Disease	9 (6.7)	-
Cancer	5 (3.7)	-
Comorbidity Burden n (%)		
≤ 3 Comorbidities (Low–Moderate)	58 (43.3)	-
≥ 4 Comorbidities (High)	76 (56.7)	-
Number of Comorbidities	-	4 (0–8)
Medications n (%)		
Analgesics	90 (67.1)	-
Proton pump inhibitors	63 (47.0)	-
Laxatives	19 (14.2)	-
CNS-acting medications	16 (11.9)	-
Polypharmacy n (%)		
≤ 5 Medications	67 (50)	-
≥ 6 Medications	67 (50)	-
Number of Medications		5.50 (0–10)
Laboratory Parameters	Mean±SD	Median (min-max)
Hemoglobin (g/dL)	-	12.35 (8.6–16.0)
MCV (fL)	-	91 (64–106)
Iron (µg/dL)	-	61 (20–185)
Ferritin (ng/mL)	-	46.0 (5.6–372.1)
Vitamin B12 (pg/mL)	-	306.5 (82–2000)
Folate (ng/mL)	-	7.34 (1.5–24.0)
Glucose (mg/dL)	-	5.95 (4.6–9.6)

ADL, dependency in daily activities ; CRP, C-Reactive Protein; GDS, Geriatric Depression Scale; MCV,Mean Corpuscular Volume; MNA-SF, Mini Nutritional Assessment ; TSH,Thyroid Stimulating Hormone; SD , standard deviation; Antidepressants and antipsychotics were grouped as CNS-acting medications.

Analgesics included paracetamol, NSAIDs, and opioid analgesics.

Anemia was defined as hemoglobin <12 g/dL for females and <13 g/dL for males.

Table 1. Continued.

Laboratory Parameters	Mean±SD	Median (min-max)
Urea (mg/dL)	45.98±16.80	-
Creatinine (mg/dL)	1.02±0.299	-
Uric acid (mg/dL)	-	5.8 (2.0–11.8)
Albumin (g/L)	-	38.6 (26.2–88.0)
TSH (µIU/mL)	-	1.35 (0.0–18.2)
Vitamin D (ng/mL)	-	11.62 (4.2–54.7)
CRP (mg/L)	-	3.55 (0.1 –141.4)
Anemia status n (%)		
Female	43 (52.4)	-
Male	26 (50.0)	-
Total	69 (51.5)	-

ADL, dependency in daily activities ; CRP, C-Reactive Protein; GDS, Geriatric Depression Scale; MCV,Mean Corpuscular Volume; MNA-SF, Mini Nutritional Assessment ; TSH,Thyroid Stimulating Hormone; SD , standard deviation; Antidepressants and antipsychotics were grouped as CNS-acting medications.

Analgesics included paracetamol, NSAIDs, and opioid analgesics.

Anemia was defined as hemoglobin <12 g/dL for females and <13 g/dL for males.

Table 2. Comparison of patient characteristics based on anemia status.

(n=134)	No anemia (n=65)	Anemia (n=69)	p
Age (years) ^a	84.68 ± 3.14	86.36 ± 4.32	0.048 ^t
Gender n (%)			0.783
Female	39 (60.0)	43 (62.3)	
Male	26 (40.0)	26 (37.7)	
n (%)			
Alone (Living Status)	14 (21.5)	17 (24.6)	0.637
Dependency (ADL)	27 (41.5)	38 (55.1)	0.117
Malnutrition(MNA-SF)	13 (20.0)	14 (20.3)	0.967
Depressive Symptoms (GDS)	26 (40.0)	33 (47.8)	0.362
Comorbid disease n (%)			
Hypertension	52 (80.0)	59 (85.5)	0.398
Dementia	20 (30.8)	22 (31.9)	0.889
Diabetes Mellitus	15 (23.1)	20 (29.0)	0.486
Congestive Heart Failure	12 (18.5)	13 (18.8)	0.955
Chronic Obstructive Pulmonary Disease	9 (13.8)	9 (13.0)	0.892
Parkinson's Disease	5 (7.7)	7 (10.1)	0.619
Cerebrovascular Disease	4 (6.2)	5 (7.2)	0.412
Cancer	1 (1.5)	4 (5.8)	0.196

ADL, dependency in daily activities ; CRP, C-Reactive Protein; GDS, Geriatric Depression Scale; MCV,Mean Corpuscular Volume; MNA-SF, Mini Nutritional Assessment ; TSH,Thyroid Stimulating Hormone;

SD, standard deviation; ^a, mean ± standard deviation; ^b, median (minimum–maximum).

^t, Student's t-test; m, Mann–Whitney U; χ^2 , Chi-square test

Antidepressants and antipsychotics were grouped as CNS-acting medications.

Analgesics included paracetamol, NSAIDs, and opioid analgesics.

Anemia was defined as hemoglobin <12 g/dL for females and <13 g/dL for males.

Table 2. Continued.

(n=134)	No anemia (n=65)	Anemia (n=69)	p
Comorbidity Burden n (%)			
≤ 3 Comorbidities	37(56.9)	21(30.4)	0.002 χ^2
≥ 4 Comorbidities	28(43.1)	48(69.6)	
Total Number of Comorbidities ^b	3 (0-8)	4 (0-7)	0.008 m
Medications n (%)			
Analgesics	40 (61.5)	50 (72.5)	0.178
Proton pump inhibitors	29 (44.6)	34 (49.3)	0.589
Laxatives	9 (13.8)	10 (14.5)	0.944
CNS-acting medications	6 (9.2)	10 (14.5)	0.348
Polypharmacy n (%)			
≤ 5 Medications	42 (64.6)	25 (36.2)	0.001 χ^2
≥ 6 Medications	23 (35.4)	44 (63.8)	
Total Number of Medications ^b	5 (0-8)	6 (0-10)	0.001m
Laboratory Parameters			
Hemoglobin ^b	13.5 (12.1 –16.0)	11.4 (8.6 –13.0)	<0.01m
MCV ^b	91.0 (64.7 –103.0)	91.0 (64.0 –106.0)	0.839
Iron ^b	69 (23 –185)	56 (20 –155)	0.008m
Ferritin ^b	45.7 (5.6 –249.8)	46.3 (8.2 –372.1)	0.732
Vitamin B12 ^b	312 (133 –2000)	304 (82 –1289)	0.650
Folate ^b	7.71 (3.2 –24)	6.61 (1.5 –24)	0.064
Glucose ^b	126(85-229)	123 (97 –212)	0.223
Urea ^a	43.4±17.15	48.4±16.21	0.019t
Creatinine ^a	0.98±0.25	1.05±0.33	0.268
Uric acid ^b	5.9 (2 –11.8)	5.6 (2.4 –10.3)	0.322
Albumin ^b	39.0 (31 –45.9)	36.7 (26.2 –88)	0.092
TSH ^b	1.34 (0 –18.2)	1.37 (0 –10.0)	0.904
Vitamin D ^b	10.4 (4.2 –54.7)	15.7 (4.2 –54.5)	0.097
CRP ^b	4.01 (0.1 –36.2)	2.67 (0.1 – 141.4)	0.268

ADL, dependency in daily activities ; CRP, C-Reactive Protein; GDS, Geriatric Depression Scale; MCV,Mean Corpuscular Volume; MNA-SF, Mini Nutritional Assessment ; TSH,Thyroid Stimulating Hormone;

SD, standard deviation; ^a, mean ± standard deviation; ^b, median (minimum–maximum).

t ,Student's t-test; m, Mann–Whitney U; χ^2 , Chi-square test

Antidepressants and antipsychotics were grouped as CNS-acting medications.

Analgesics included paracetamol, NSAIDs, and opioid analgesics.

Anemia was defined as hemoglobin <12 g/dL for females and <13 g/dL for males.

Logistic regression analysis

A statistically significant negative correlation was observed between hemoglobin level and the number of medications (Spearman's ρ = -0.230, p = 0.008) as well as the number of comorbidities (Spearman's ρ = -0.227, p = 0.008) (Table 3).

Logistic regression analyses were performed to identify factors associated with anemia. In univariable analyses, age, polypharmacy, and comorbidity burden were significantly associated with anemia (p < 0.05). Sex, malnutrition, and urea level were not statistically significant but

were retained in multivariable modeling due to their established clinical relevance. Given the high correlation between medication count and comorbidity count ($r = 0.765$), these variables were analyzed in separate multivariable models to avoid multicollinearity.

In Model 1 (including polypharmacy), age (OR = 1.166; 95% CI: 1.053–1.291; $p = 0.003$) and polypharmacy (OR = 4.051; 95% CI: 1.892–8.676; $p < 0.001$) were independently associated with anemia. In Model 2 (including comorbidity count), age (OR = 1.126; 95% CI: 1.022–1.240; $p = 0.017$) and comorbidity burden (OR = 2.950; 95% CI: 1.430–6.088; $p = 0.003$) remained independently associated with anemia. The Hosmer–Lemeshow test indicated adequate model fit for both models (Model 1: $p = 0.125$; Model 2: $p = 0.516$) (Table 4).

Table 3. Correlation of hemoglobin with number of medications and comorbidities.

	Spearman's rho (r)	p
Number of medications	-0.230	0.008
Number of comorbidities	-0.227	0.008

A p value < 0.05 was considered statistically significant.

Discussion

This study demonstrated that anemia is common among individuals aged 80 years and older and is associated with both comorbidity burden and polypharmacy. The findings suggest that considering these factors in the evaluation of anemia in very old adults may be meaningful.

With aging, decreases in physiological reserves, chronic low-grade inflammation, vascular stiffness, and metabolic changes are among the key mechanisms that increase the frequency of cardiovascular diseases. These processes are known to be closely related to the rise in hypertension and multimorbidity prevalence in advanced age.^[15] Indeed, the literature reports that the prevalence of hypertension in older adults exceeds 70%^[16] and that multiple chronic disease burden is common. Similarly, in older populations with cardiovascular disease, the proportion of individuals with four or more comorbidities has been reported to be approximately 50%.^[4] Consistent with these findings, hypertension was the most frequently observed chronic condition in our study (82.8%). In addition, the presence of four

Table 4. Logistic regression analysis of factors associated with anemia.

		Univariate						Multivariable				
Model 1	β	OR	95% CI			p	β	OR	95% CI			p
Age	0.118	1.126	1.025		1.237	0.013	0.154	1.166	1.053	-	1.291	0.003
Gender	0.098	0.907	0.453	-	1.818	0.783						
Polypharmacy	1.167	3.214	1.585	-	6.516	<0.001	1.399	4.051	1.892	-	8.676	<0.001
Malnutrition	0.018	1.018	0.437	-	2.370	0.967						
Urea	0.019	1.019	0.997	-	1.041	0.090						
Model 2												
Age	0.118	1.126	1.025		1.237	0.013	0.126	1.126	1.022	-	1.240	0.017
Gender	0.098	0.907	0.453	-	1.818	0.783						
High comorbidity burden	1.070	2.916	1.439	-	5.911	0.003	1.082	2.950	1.430	-	6.088	0.003
Malnutrition	0.018	1.018	0.437	-	2.370	0.967						
Urea	0.019	1.019	0.997	-	1.041	0.090						

OR, odds ratio; CI, confidence interval. The dependent variable was anemia status.

Model 1: Included age, sex, polypharmacy (≥ 6 medications), malnutrition, and urea (Hosmer–Lemeshow $p = 0.125$).

Model 2: Included age, sex, comorbidity burden (≥ 4 comorbidities), malnutrition, and urea (Hosmer–Lemeshow $p = 0.516$).

Variable selection in both models was performed using the forward likelihood ratio method

or more comorbidities in 56.7% of the participants reflects a high multimorbidity burden and is in line with the existing literature.

It is well recognized that medication use increases substantially in parallel with an increasing number of comorbidities. In the literature, approximately 56% of individuals aged 85 years and older are reported to use five or more medications; among individuals with two comorbid diseases, 20.8% reportedly use 4–9 medications and 1.1% use ten or more.^[5] These data suggest a relationship between multimorbidity and polypharmacy in advanced age. In line with these findings, polypharmacy (use of six or more medications) was identified in 50% of participants in our study. Additionally, the high prevalence of analgesic use may be related to musculoskeletal problems and chronic pain, which are common in advanced age.^[17]

In this study, anemia prevalence among individuals aged 80 years and older was 51.5%. This rate suggests that anemia is a common clinical problem in very old adults and is generally consistent with the high prevalence rates reported in the literature. Similarly, studies conducted among older adults receiving home healthcare services have reported high anemia prevalence. Aslaner et al. reported an anemia prevalence of 58.7% in this group^[18], while in a prospective cohort study by Yurt and Yavuz, the prevalence was 65.4% among older adults receiving home care.^[19] Although lower prevalence rates have been reported in community-dwelling older adults, rates exceeding 50% appear consistent with the literature in groups with higher healthcare needs.^[2]

It has been reported that the high prevalence of anemia in older adults may be associated with multiple factors, including age-related physiological changes, chronic inflammation, physical inactivity, polypharmacy, nutritional deficiencies, and an increased comorbidity

burden.^[2] In this respect, the advanced age of the study population, high comorbidity burden, and prevalent polypharmacy may be considered among the factors contributing to the observed frequency of anemia.

The presence of multimorbidity has been explained by various biological mechanisms that may be associated with the development of anemia in advanced age. It has been reported that low-grade chronic inflammation accompanying an increased chronic disease burden may contribute to the development of inflammation-related anemia by suppressing erythropoiesis and disrupting iron metabolism.^[3] In this context, the finding in our study that anemia was independently associated with comorbidity burden may be considered consistent with these mechanisms. Indeed, some studies have reported that the likelihood of developing anemia increases progressively in individuals with two or more comorbidities, and that this increasing trend becomes more pronounced particularly in the presence of three or more comorbidities.^[9,18] Similarly, in our study, the presence of four or more comorbidities was found to be significantly associated with anemia. This threshold is consistent with previous studies as a marker reflecting clinical vulnerability.^[8]

In our study, the finding that urea levels were higher and iron levels were lower in anemic individuals suggests that impaired renal function and alterations in iron metabolism may contribute to the development of anemia. Indeed, the literature has shown that blood urea nitrogen is inversely associated with hemoglobin levels, independent of glomerular filtration rate.^[20] On the other hand, previous studies have reported that iron deficiency and other nutritional deficiencies play a role in the etiology in approximately one third of older adults with anemia, while chronic inflammation or chronic kidney disease contributes to the etiology in another one third.^[21]

However, in our study, no statistically significant association was found between malnutrition and anemia. This finding may be related to the fact that the screening tool used (MNA-SF) does not directly include hematological parameters, the multifactorial nature of anemia, and the relatively low prevalence of malnutrition in the study population. On the other hand, the positive association observed between iron levels and hemoglobin suggests that the role of nutritional deficiency in the development of anemia cannot be completely excluded.^[22] This observation implies that, when evaluating anemia in older adults, incorporating biochemical parameters alongside general nutritional screening tools may be helpful.

Polypharmacy is considered one of the important clinical factors that may be associated with the development of anemia in advanced age. In the literature, it has been reported that multiple medication use may be associated with anemia through mechanisms such as gastrointestinal adverse effects, impaired nutrient absorption, and chronic inflammation. In particular, nonsteroidal anti-inflammatory drugs, anticoagulants, and certain cardiovascular medications have been reported to increase the risk of gastrointestinal mucosal damage and occult bleeding, while medications such as proton pump inhibitors and metformin may affect iron and vitamin B12 absorption.^[2] Within this framework, the identification of analgesics as the most frequently used medication group in our study may be compatible with potential gastrointestinal mechanisms described in the literature. In parallel, the independent association between polypharmacy and anemia suggests that medication burden should be considered during anemia assessments in very old adults. Nonetheless, further detailed and prospective studies are needed to clarify the specific effects of medication types, duration of use, and combinations on this relationship.

This study has several limitations. First, its single-center design and relatively limited sample size may affect generalizability. In addition, the study population consisted of individuals registered in the Healthy Aging Program and followed in a dedicated outpatient/home-care setting. Therefore, the participants may represent a selected group of adults aged 80 years and older with relatively higher healthcare needs than the general community-dwelling older population. This should be considered when extrapolating the findings to broader older adult populations or to different primary care settings. Consecutive sampling helps reduce selection bias by the researchers, but it may limit how well the results apply to other populations because only program-registered individuals were included. Due to the cross-sectional design, observed associations cannot be interpreted causally. No sub-classification of anemia etiology was performed. Furthermore, while the sample size was adequate to evaluate the cumulative burden of comorbidity, it was insufficient to analyze the specific associations between anemia and individual disease subtypes (e.g., different types of neoplasms) or specific drug classes. Additionally, the fact that some clinical data were obtained from primary caregivers may have modestly affected data accuracy.

Despite these limitations, the study's focus on individuals aged 80 years and older and the combined evaluation of comorbidity and polypharmacy, based on real-world data, may contribute to a better understanding of the clinical characteristics of this patient group in our country.

Conclusion

This study indicates that anemia is commonly observed among individuals aged 80 years and above and appears to be associated with a higher burden of comorbidities and increased medication use. These observations highlight the potential value of assessing anemia within a broader

clinical context, which includes consideration of existing comorbidities and polypharmacy, to inform a more comprehensive and individualized care approach in very old adults. From a primary care perspective, these findings suggest that anemia in adults aged 80 years and older should not be evaluated solely as an isolated laboratory abnormality. When anemia is detected in this age group, clinicians should also consider reviewing the patient's comorbidity burden, medication list, renal function, nutritional indicators, and potential drug-related contributors. In particular, the presence of polypharmacy may serve as a practical warning sign prompting medication review and assessment of potentially reversible causes of anemia.

Ethical approval

This study has been approved by the Amasya University Non-Interventional Clinical Research Ethics Committee (approval date 28.04.2025 number E-76988455-050.04-258208). Written informed consent was obtained from the participants.

Author contribution

The authors declare contribution to the paper as follows: Study conception and design: AD, SBŞ; data collection: AD, SBŞ; analysis and interpretation of results: AD, SBŞ; draft manuscript preparation: AD, SBŞ. All authors reviewed the results and approved the final version of the article.

Source of funding

The authors declare the study received no funding.

Conflict of interest

The authors declare that there is no conflict of interest to disclose.

References

1. World Health Organization (WHO). Nutritional anaemias: report of a WHO scientific group. Geneva: WHO; 1968.
2. Stauder R, Valent P, Theurl I. Anemia at older age: etiologies, clinical implications, and management. *Blood*. 2018;131:505-514. [\[Crossref\]](#)
3. Girelli D, Marchi G, Camaschella C. Anemia in the elderly. *Hemasphere*. 2018;2:e40. [\[Crossref\]](#)
4. Forman DE, Maurer MS, Boyd C, et al. Multimorbidity in older adults with cardiovascular disease. *J Am Coll Cardiol*. 2018;71(19):2149-2161. [\[Crossref\]](#)
5. Aggarwal P, Woolford SJ, Patel HP. Multi-morbidity and polypharmacy in older people: challenges and opportunities for clinical practice. *Geriatrics (Basel)*. 2020;5:85. [\[Crossref\]](#)
6. Thompson W, McDonald EG. Polypharmacy and deprescribing in older adults. *Annu Rev Med*. 2024;75:113-127. [\[Crossref\]](#)
7. Peduzzi P, Concato J, Kemper E, Holford TR, Feinstein AR. A simulation study of the number of events per variable in logistic regression analysis. *J Clin Epidemiol*. 1996;49:1373-1379. [\[Crossref\]](#)
8. Holzer BM, Siebenhuener K, Bopp M, Minder CE. Overcoming cut-off restrictions in multimorbidity prevalence estimates. *BMC Public Health*. 2014;14:780. [\[Crossref\]](#)
9. Michalak SS, Rupa-Matysek J, Gil L. Comorbidities, repeated hospitalizations, and age ≥ 80 years as indicators of anemia development in the older population. *Ann Hematol*. 2018;97:1337-1347. [\[Crossref\]](#)
10. Masnoon N, Shakib S, Kalisch-Ellett L, Caughey GE. What is polypharmacy? A systematic review of definitions. *BMC Geriatr*. 2017;17:230. [\[Crossref\]](#)
11. Arik G, Varan HD, Yavuz BB, et al. Validation of Katz index of independence in activities of daily living in Turkish older adults. *Arch Gerontol Geriatr*. 2015;61:344-350. [\[Crossref\]](#)
12. Sarikaya D, Halil M, Kuyumcu ME, et al. Mini nutritional assessment test long and short form are valid screening tools in Turkish older adults. *Arch Gerontol Geriatr*. 2015;61:56-60. [\[Crossref\]](#)
13. Ertan T, Eker E. Reliability, validity, and factor structure of the geriatric depression scale in Turkish elderly: are there different factor structures for different cultures? *Int Psychogeriatr*. 2000;12:163-172. [\[Crossref\]](#)
14. Hosmer DW, Lemeshow S, Sturdivant RX. Applied logistic regression. 3rd ed. New York: Wiley; 2013. [\[Crossref\]](#)

15. North BJ, Sinclair DA. The intersection between aging and cardiovascular disease. *Circ Res.* 2012;110:1097-1108. [\[Crossref\]](#)
16. Oliveros E, Patel H, Kyung S, et al. Hypertension in older adults: assessment, management, and challenges. *Clin Cardiol.* 2020;43:99-107. [\[Crossref\]](#)
17. Tevik K, Benth JS, Aarøen M, Lornstad MT, Bergh S, Helvik AS. Prevalence and persistent use of analgesic drugs in older adults receiving domiciliary care at baseline-A longitudinal study. *Health Sci Rep.* 2021;4:e316. [\[Crossref\]](#)
18. Aslaner H, Nursoy N, Aslaner HA. Anemia in the elderly receiving home healthcare service: association with their functional. *Medical Records.* 2025;7:603-608. [\[Crossref\]](#)
19. Yurt N, Yavuz E. Anemia is associated with mortality and higher hospitalization rates in elderly patients receiving home care: a prospective cohort study. *Eurasian Journal of Family Medicine.* 2024;13:7-15. [\[Crossref\]](#)
20. Kim HJ, Kim TE, Han M, et al. Effects of blood urea nitrogen independent of the estimated glomerular filtration rate on the development of anemia in non-dialysis chronic kidney disease: The results of the KNOW-CKD study. *PLoS One.* 2021;16:e0257305. [\[Crossref\]](#)
21. Guralnik JM, Eisenstaedt RS, Ferrucci L, Klein HG, Woodman RC. Prevalence of anemia in persons 65 years and older in the United States: evidence for a high rate of unexplained anemia. *Blood.* 2004;104:2263-2268. [\[Crossref\]](#)
22. İncedal Sonkaya Z, Kurtgöz A. Anaemia, iron, and vitamin D deficiency in the elderly: a retrospective review. *Journal of Geriatric Science.* 2023;6:14-19. [\[Crossref\]](#)