

ORIGINAL RESEARCH

Clinicopathological profile of anaemia in geriatric patients

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ABSTRACT

Background: Anaemia is typically defined as reduction in the haemoglobin concentration below certain value. It is a commonly encountered haematological problem in the elderly causing significant morbidity and mortality. Ageing populations will impact on healthcare provision, and hence, it is important to identify and understand the significance of common medical problems in older people of which anaemia is one such problem. **Aims and Objectives:**

1. To study the clinicopathological profile of anemia in geriatric patients.
2. To determine the various causes of anemia in geriatric patients.

Materials and Methods: This study was conducted on patients who were above 60 years of age and was conducted at Department of Medicine, Government Medical College, Amritsar. It was a cross sectional study of 100 patients. It males having haemoglobin levels of less than 13 gm/dl and Females having haemoglobin levels of less than 12 gm/dl. The patients having haematological disorders and liver disorders were excluded from the study. **Results:** An association between age and grading of anemia was observed ($p > 0.001$). 100% patients with ≤ 70 years mild anemia followed by 81.6% had moderate anemia and 58.6% severe anemia. On the other hand, 18.4% and 41.4% patients with age > 70 years had moderate and severe anemia. About 31.8% females were having mild anemia followed by 49% with moderate anemia and 41.4% with severe anemia. On the other hand, 68.2%, 51% and 58.6% patients had mild, moderate and severe anemia. No association between gender and grading of anemia was observed ($p > 0.393$). **Conclusion :** Anaemia in older persons poses a clinical challenge in daily practice as the population ages. It was concluded that majority of geriatric patients with anemia in the present study were < 70 years. Common symptoms among them were fatigue, weakness and breathlessness and had high association with anemia.

Key Words:

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INTRODUCTION

Anaemia is typically defined as reduction in the haemoglobin concentration below certain value. The pathophysiology of ACD is complex and involves a functional iron shortage brought on by a decreased ability of red blood cells to recycle iron. The bone marrow exhibits increased erythroid progenitor cell death, insufficient erythropoietin (EPO) synthesis, and a compromised response to EPO. ACD may be caused by high levels of pro-inflammatory cytokines such TNF α , IL-6, IL-1, and macrophage migration inhibitory factor (MIF), with IL-6's stimulation of hepcidin production serving as a major mediator. Hepcidin causes an iron-restrictive anemia by preventing the intestines from absorbing iron and by preventing macrophages from releasing recycled iron.⁶

MATERIAL AND METHODS

This study was conducted on patients who were above 60 years of age and was conducted at Department of Medicine, Government Medical College, Amritsar

Design of study –

1. Cross sectional Study
2. Sample Size - 100 patients.
3. Duration - 12 months.

INCLUSION CRITERIA

Age ≥ 60 years

Male having haemoglobin levels of less than 13 gm/dl and Females having haemoglobin levels of less than 12 gm/dl.

EXCLUSION CRITERIA

Age < 60 years

Those who had known haematological disorders

Those who had known liver disorders.

Bone marrow examination

Stool examination

Bowel examination

METHODS OF DATA COLLECTION: A detailed case history was taken in all patients & meticulous clinical examination was done as per Performa.

THE INVESTIGATION CONDUCTED:

Complete blood count,

Peripheral blood smear (L.G stain)

OTHER INVESTIGATIONS:

Iron Studies

Vitamin B12 and folate

STATISTICAL ANALYSIS:

At the end of study, the data was collected and analyzed using appropriate statistical methods. The statistical software SPSS was used for statistical analysis. The mean \pm standard deviation was calculated. Pair- wise comparison between the cases was performed for all parameters using Student's unpaired t-test. The values of $P < 0.05$ was considered as significant. The qualitative variables were compared using the chi-square test. Univariate correlation analysis was used to confirm the significance of the variables.

RESULTS**Parameters**

Parameters	No.	Mean	Standard Deviation	Minimum	Maximum
Age	100	67.25	7.050	60	87
HB	100	8.380000	1.7027014	5.7000	11.6000
MCV	100	84.52	14.928	56	122
WBC count	100	8595.38	2657.331	2344	16987
Platelet Count	100	270876.22	103107.765	76890	492345
Reticulocyte Count	100	1.923000	.6780625	.2000	3.6000
S. FERRETIN	100	120.92	114.272	12	376
S. Iron	100	67.75	44.664	13	146
Tf Saturation	100	29.94	13.409	17	139
TIBC	100	347.90	50.190	125	450
Vit B12	100	593.91	786.493	87	7865
Blood Urea	100	37.87	16.907	16	98
Serum Creatinine	100	1.253100	.7107241	.7000	4.1000
Serum Bilirubin	100	.863000	.8356519	.1000	4.2000
S.LDH	100	218.28	66.848	141	452

Table 12: Mean was calculated for all the parameters among the patients. It was noticed that mean age was 67.25 years, mean HB-8.38 which was quite low, mean MCV-84.52, mean WBC count-8595.38, mean platelet count-270876.22, mean Reticulocyte count-

1.92, mean serum ferritin-120.9, mean serum Iron-67.75, mean Tf saturation-29.94, mean TIBC-347.9, mean Vit B12-593.91, mean Blood urea-37.87, mean S. creatinine-1.25, mean serum Bilirubin-0.86 and mean S.LDH-218.28.

Age and Grading of Anaemia

	Grading Of Anaemia			Total
	Mild	Moderate	Severe	
≤ 70	22	40	17	79
	100.0%	81.6%	58.6%	79.0%
> 70	0	9	12	21
	.0%	18.4%	41.4%	21.0%
Total	22	49	29	100
	100.0%	100.0%	100.0%	100.0%
Pearson's chi square- 13.313; df- 2; p value- 0.001				

Table 13: An association between age and grading of anemia was observed ($p > 0.001$). 100% patients with ≤ 70 years mild anemia followed by 81.6% had

moderate anemia and 58.6% severe anemia. On the other hand, 18.4% and 41.4% patients with age > 70 years had moderate and severe anemia.

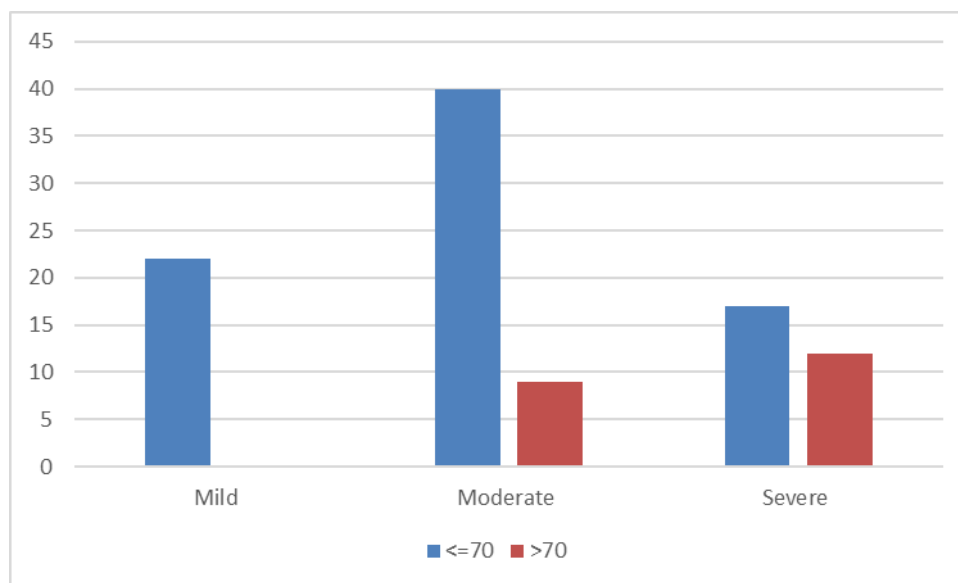


Figure 13: Age vs grading of Anemia

DISCUSSION

Anemia is a disorder characterized by a decreased blood potential to carry oxygen because of a drop in hemoglobin concentration or red blood cell count. The production of the biological components of blood, such as red blood cells (RBCs), is the principal function of the hematopoietic machinery located in the bone marrow. The well-organized operation of bone marrow is dependent on endogenous substances including iron, vitamin B12, folic acid, trace elements (copper, cobalt, manganese), and growth factors like erythropoietin and G-CSF. Therefore, any disruption in this machinery's functioning, whether brought on by a lack of resources or long-term bone marrow disorders, results in anemia, especially in the geriatric group.

Age was stratified into different age groups. It was found that 79% patients were in ≤ 70 years of age group while 21% were under >70 age group. Mean age was 67.25 ± 7.05 . Another study revealed that the age group of the patients ranged from 60 – 98 years. The mean age was found to be 68.90 years with the maximum patients in 61-70 years age group.⁵³ The mean age distribution of anaemia in elderly in our study was 73.5 years. 68% of elderly with anaemia were between the age group of 60-70 years and 32% were between the age group of 70-88 years.⁶⁵ In a study done by Bhasin et al., 2011⁴⁷ the mean age was found to be 70.51 years. Mean age of elderly patients was found to be 68.5 years, with maximum patients in 61-71 age group. The age group of patients ranged from 61-100 years.⁵⁴ Maximum number of patients, 24 (40%) were in the age group 65-69 years.⁶⁶ Anaemia has been found to occur in both men and women above 65 years of age. A definite cause or causes are associated with anaemia in this age group. Evidently, anaemia in old age is not due to the physiological process of ageing; rather it is associated with a disease process seen in old age [Raina et al.,

2014].⁶⁷ Aithal et al., 2017⁵⁵ observed that 70 patients were between the ages of 60 to 69 years, 23 patients between 70 to 79 years, 7 patients above 80 years. Ok et al., 2023⁶³ observed that the mean \pm SD age was 67.6 ± 6.6 years.

Present study found that males (57%) outnumbered the females (43%). Khatib et al., 2016⁵³ observed that majority of patients were males with 138 (53.90%) cases while females accounted for 118 (46.09%) cases. Study by Guralink et al., 2004¹⁷ also showed a male preponderance. However, there are other studies such as Shrivastava et al., 2013⁷⁰ which revealed female preponderance. Narayanaswami et al., 2015⁶⁵ also observed that males (85%) prevalence was higher than females (42%). According to Vojjala and Paul (2017),⁵⁴ males constituted 71% of the population while females, at 58, were less in number than males (142). Sfurti Mann, et al. [2014]⁶⁶ conducted a study on 42 patients (70%) were male and 18 patients (30%) were female. 100 patients were included in the study by Aithal et al., 2017,⁵⁵ of which 76 were male and 24 were females. Ok et al., 2023⁶³ noticed that more than half of the elderly with anemia (53.7%) were of male gender with M:F ratio of 1.2:1. Studies conducted by Talukdar et al, 2022,⁷¹ Rogrig et al, 2016⁷² had shown female preponderance (F:M=1.9:1), 67.5% respectively.

In our study, Fatigue is one of the symptoms reported by the patients. It was observed that 42% patients did not have fatigue while 58% showed this symptom. Weakness was also recorded among the patients. It was noticed that 54% patients had weakness while 46% showed no symptoms of weakness. About 35% patients showed that breathlessness was one of the symptoms present while 65% did not report breathlessness. Majority of patients (82%) did not report that pedal edema in them. On the other hand, 18% showed to have pedal edema. Stool examination showed that only 3% cases had ova in their stool

while 97% had normal stools. Pallor and generalized weakness were seen in all patients, whereas dyspnoea, fever and pedal oedema were seen in 88.1, 61.9 and 53.6% cases, respectively. The dominant presentation was considered among which the most common presentation was generalised weakness which constituted to 35% (70) followed by breathlessness which constituted to 27.5% [Vojjala and Paul, 2017].⁵⁴ Prakash, et al. [2015],⁵² it is easy to overlook anaemia in the elderly, since such symptoms as fatigue, weakness, or shortness of breath may be attributed to the aging process itself. Ok et al., 2023 also reported generalized weakness/ fatigue, palpitation, headache, fever and pedal oedema as common complaints. In the present study, 100% cases in which fatigue was not recorded had mild anemia followed by 40.8% with moderate anemia. On the other hand, those who had fatigue were 59.2% with moderate and 100% with severe anemia. Highly association between fatigue and grading of anemia was observed ($p>0.000$).

90.9% cases in which weakness was not recorded had mild anemia followed by 46.9% with moderate and 10.3% with severe anemia. On the other hand, those who had weakness were 9.1% with mild anemia, 53.1% with moderate and 89.7% with severe anemia. A statistically significant association between weakness and grading of anemia was observed ($p>0.000$). 95.5% cases in which breathlessness was not recorded had mild anemia followed by 85.7% with moderate and 6.9% with severe anemia. On the other hand, those who had breathlessness were 4.5%, 14.3 and 93.1% with mild, moderate and severe anemia. This association between breathlessness and grading of anemia was observed ($p>0.000$).

In the present study, stool examination showed that only 17% cases had ova in their stool while 83% had normal stools. 81.8% cases in which stool examination was normal had mild anemia followed by 91.8% with moderate and 68.9% with severe anemia. On the other hand, in which ova was seen were 18.2%, 8.16% and 31% had mild, moderate and severe anemia, respectively. This association was found to be significant ($p>0.030$). Stool examination for occult blood was done in 56 patients and 8 were positive for the same.⁷³

Present study calculated grading of anemia according WHO guidelines. It was found that maximum patients (49%) were having moderate anemia, followed by severe anemia in which 29% patients were there. 22% patients had mild anemia. Majority of the anaemia was in moderate category that is 8-10.9 gm/dl, both for male and female groups (male = 38, 57.6%, female = 43, 75.4) [Ok et al., 2023].⁶³ Study by Gangadharan et al. [2016]⁷⁴ found that men had predominantly mild anaemia while in women moderate anaemia was more common. According to Hassan et al. (2020),⁵⁸ the majority of our patients—39 instances, or 65%—presented with moderate anemia, followed by 11 cases (18.33%) with severe

anemia and 10 cases (16.67%) with mild anemia. Similar results were given by Kandhiravan et al., 2023. They observed that among 154 patients with anemia, majority 68 (44.2%) had mild anemia, followed by moderate anemia in 57 (37%) participants. Severe anemia affected around one-fifth of the elderly.⁷⁵

Majority of our patients (39 cases, 65%) were presented with moderate anemia followed by 11 cases (18.33%)

with severe anemia and 10 cases (16.67%) with mild Peripheral blood smear showed that 38% cases were having microcytic anemia, 16% had normocytic anemia, 38% had Normocytic normochronic anaemia, 7% were having dimorphic anemia and 1% had pancytopenia category. About 40.9% cases had mild anemia fell under category Normocytic normochronic anaemia. Those who had moderate anemia was in category Normocytic normochronic anaemia (40.8%) and those who had severe anemia were again in category Normocytic normochronic anaemia. However, the association was borderline significant ($p>0.051$).

Morphological classification of anemia revealed that most of our cases had normocytic anemia (45 cases, 75%) followed by 13 cases (21.7%) of microcytic anemia and only 2 cases (3.3%) of macrocytic anemia.⁵⁸ It is noteworthy to mention that anaemia of chronic disease or disorder is the most common anaemia in elderly. This type of anaemia associated with a number of conditions, such as acute infections, chronic infections (e.g., tuberculosis), chronic inflammatory disorders (e.g., rheumatoid disease and osteoarthritis), and malignancy. Agravat et al., 2021⁶¹ also suggested that the most common morphological type of anemia was normocytic normochromic (45%) followed by hypochromic microcytic (29.4%), dimorphic (16.7%), normocytic hypochromic anemia (5.4%), and macrocytic (3.5%), which was the least common.

In our study, bone marrow examination showed that majority of patients had normal results while 7% had hypercellular bone marrow and 5% had hypocellular bone marrow. About 9.1% cases with hypercellular bone marrow had mild anemia followed by 10.2% with moderate anemia. Those who had hypocellular bone marrow were 17.2% and had severe anemia. Normal bone marrow was seen in 90.9% cases with mild anemia, 89.8% with moderate and 82.8% with severe anemia. However, the association was significant ($p>0.004$).

Whole abdomen ultrasound showed that 87% patients have normal USG followed by 7% have splenomegaly and 6% have contracted Kidneys. About 90.9%, 85.7% and 86.2% cases had mild, moderate and severe anemia underwent normal USG. On the other hand, 9.1% and 10.2% had mild and moderate anemia, respectively have splenomegaly on USG. Similarly, 4.1% had moderate anemia and 13.8% had

severe anemia have contracted kidneys on USG. However, the association was not significant ($p > 0.004$). The commonest cause for anemia of chronic disease in a study was chronic kidney disease (40%) [Krishnamurthy et al., 2022].⁷⁵ Anaemia of chronic disease constitutes one-third of the aetiology of anaemia in patients >65 years of age. Despite normal or increased iron reserves, there are decreased circulating blood iron levels in this situation.

In our study, mean was calculated for all the parameters among the patients. It was noticed that mean age was 67.25 years, mean HB-8.38 which was quite low, mean MCV-84.52, mean WBC count-8595.38, mean platelet count-270876.22, mean Reticulocyte count- 1.92, mean serum ferritin-120.9, mean serum Iron-67.75, mean Tf saturation-29.94, mean TIBC-347.9, mean Vit B12-593.91, mean Blood urea-37.87, mean S. creatinine-1.25, mean serum Bilirubin-0.86 and mean S.LDH-218.28. In our study, analysis between clinical parameters and grading of anemia was done. It was observed that age, Hb, MCV, serum iron, TIBC, blood urea and serum creatinine showed highly significant association with grading of anemia. Forty-nine patients with iron and dual deficiency anemia had low serum ferritin levels. Increased value was observed in 28 cases of anaemia of chronic diseases, whereas three cases had normal value. The serum ferritin levels were below 15 $\mu\text{g/l}$ in patients with iron deficiency anaemia, whereas patients with chronic disease had serum ferritin levels greater than 300 $\mu\text{g/l}$ [Raina et al., 2014].⁷⁶ Iron deficiency anaemia was the most common underlying aetiology detected, followed by Anaemia of chronic disease. 4/8 patients had VitB₁₂ deficiency confirmed by serum VitB₁₂ assays. Vitamin B12-folate deficiency was found in 8% patients [Kandhiravan et al., 2023].⁷⁵ Our study indicates that anemia resulting from chronic disease is the primary cause of anemia in the elderly. However, both anemia of chronic disease and iron-deficiency anemia, are two important causes for anemia in hospitalized elderly patients. Chronic blood loss is the most common etiology behind iron deficiency anemia.

In the present study, it was found that HB had correlation with age, MCV, TIBC, S. iron and S. creatinine. Age had correlation with HB, MCV, TIBC. MCV had association with age, HB, S.Iron, S. ferritin, Vit B12, TIBC, Tf saturation. WBC count had correlation with Rectic count, platelet count and Tf saturation. Platelet count had correlation with TIBC, WBC count and Tf saturation. Rectic count had correlation with WBC count, tf saturation, S.LDL, S. bilirubin. S. ferritin had correlation with MCV, S.Iron, Tf saturation, TIBC, blood urea and serum creatinine. S. iron had correlation with HB, MCV, S. Ferritin, tf saturation, TIBC, VitB12 and S. bilirubin. Tf saturation had correlation with MCV, WBC count, platelet count, rectic count, S.ferritin, S.iron, TIBC. TIBC had correlation with HB, Age, MVC, platelet count, S.ferritin, S.iron, Tf saturation, Vit B12, Blood

Urea, S. creatinine. VitB12 was associated with MCV, S.iron, TIBC. Blood urea had association with HB, S. ferritin, S.iron, TIBC. S. creatinine was associated with HB, S. ferritin, TIBC, blood urea. S. bilirubin showed association with rectic count, s.iron, S.LDL. S.LDL had correlation with rectic count, S.iron, S.Bilirubin. Hemoglobin concentration though slightly, was age related, a cross sectional estimated study revealed a mean yearly decline to be more pronounced in men than in women (-0.08 and -0.05 g/dl respectively $P < 0.0001$) [Bhasin et al., 2011].⁴⁷

CONCLUSION

Anaemia in older persons poses a clinical challenge in daily practice as the population ages. It was concluded that majority of geriatric patients with anemia in the present study were <70 years. Common symptoms among them were fatigue, weakness and breathlessness and had high association with anemia. All these symptoms are associated with increased risk of impaired muscle strength executive function impairment and dementia. Anaemia in maximum patients was of moderate level, mean HB was found to be 8 grams in patients and had correlation with age, MCV, TIBC, S. iron and S. creatinine. It was observed that geriatric anemia leads to increase hospital admissions and stays. Also, impairment of iron metabolism secondary to inflammation shares many laboratory abnormalities with iron deficiency such as a low mcv, serum iron level and transferrin saturation. Thus, comprehending the underlying mechanism of anaemia at old age will form the basis of individualized treatment.

REFERENCES

1. Halen Gaskell, Sheena Derry, et al. Prevalence of anaemia in older persons: systematic review; BMC Geriatrics. 2008;8:1-8.
2. Beutler E, Waalen J. The definition of anemia: What is the lower limit of normal of the blood haemoglobin concentration? Blood. 2006;107:1747-1750.
3. World Health Organization: Nutritional anaemia: report of a WHO scientific group. Geneva, Switzerland, WHO; 1968.
4. Denny SD, Kuchibhatla MN, Cohen HJ. Impact of anemia on mortality, cognition, and function in community-dwelling elderly. Am J Med. 2006;119(4):327-34.
5. Edgren G, Bagnardi V, Bellocco R, Hjalgrim H, Rostgaard K, Melbye M, et al. Pattern of declining hemoglobin concentration before cancer diagnosis. Int J Cancer. 2010;127(6):1429-36.
6. Weiss G, Goodnough LT. Anemia of chronic disease. N Engl J Med. 2005;352(10):1011-23.
7. Bach V, Schruckmayer G, Sam I, Kemmler G, Stauder R. Prevalence and possible causes of anemia in the elderly: a cross-sectional analysis of a large European university hospital cohort. Clin Interv Aging. 2014;9 1-10.
8. den Elzen WP, de Craen AJ, Wiegerinck ET, Westendorp RG, Swinkels DW, Gussekloo J. Plasma

- hepcidin levels and anemia in old age. The Leiden 85-Plus Study. *Haematologica*. 2013;98(3):448–54
9. Juárez-Cedillo T , Basurto-Acevedo L , Vega-García S , Manuel-Apolinar L , Cruz-Tesoro E , Rodríguez-Pérez JM , et al. Prevalence of anaemia and its impact on the state of frailty in elderly people living in the community: SADEM study. *Ann Hematol*. 2014;93(12):2057–62.
 10. Zakai NA, McClure LA, Prineas R, Howard G, McClellan W, Holmes CE, et al. Correlates of anemia in American blacks and whites: the REGARDS renal ancillary study. *Am J Epidemiol*. 2009; 169(3): 355–64.
 11. Sahin S, Tasar PT, Simsek H, Çicek Z, Eskiizmirli H, Aykar FS, et al. Prevalence of anemia and malnutrition and their association in elderly nursing home residents. *Aging Clin Exp Res*. 2016;28(5):857–62.
 12. Zaninetti C, Klersy C, Scavariello C, Bastia R, Baldini CL, Invernizzi R. Prevalence of anemia in hospitalized internal medicine patients: correlations with comorbidities and length of hospital stay. *Eur J Intern Med*. 2018;51:11–7.
 13. Metivier F, Marchais SJ, Guerin AP, Pannier B, London GM. Pathophysiology of anaemia: focus on the heart and blood vessels. *Nephrol Dial Transpl*. 2000;15 Suppl 3:14–8.
 14. Silverberg DS, Wexler D, Blum M, Keren G, Sheps D, Leibovitch E, et al. The use of subcutaneous erythropoietin and intravenous iron for the treatment of the anemia of severe, resistant congestive heart failure improves cardiac and renal function and functional cardiac class, and markedly reduces hospitalizations. *J Am Coll Cardiol*. 2000;35(7):1737–44.
 15. Lanier JB, Park JJ, Callahan RC. Anemia in older adults. *Am Fam Physician*. 2018;98(7):437–42.
 16. Katsumi A, Abe A, Tamura S, Matsushita T. Anemia in older adults as a geriatric syndrome: a review. *Geriatr Gerontol Int*. 2021;21(7):549–54.
 17. 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(8):2263–8.
 18. Carmel R . Anemia and aging: an overview of clinical, diagnostic and biological issues. *Blood Rev*. 2001;15(1):9–18.
 19. Joosten E , Ghesquiere B , Linthoudt H , Krekelberghs F , Dejaeger E , Boonen S , et al. Upper and lower gastrointestinal evaluation of elderly inpatients who are iron deficient. *Am J Med*. 1999;107(1): 24–9.
 20. Rockey DC , Cello JP . Evaluation of the gastrointestinal tract in patients with iron-deficiency anemia. *N Engl J Med*. 1993;329(23):1691–5.
 21. Andrès E , Federici L , Serraj K , Kaltenbach G . Update of nutrient-deficiency anemia in elderly patients. *Eur J Intern Med* 2008;19(7):488–93.
 22. Goodnough LT , Schrier SL . Evaluation and management of anemia in the elderly. *Am J Hematol*. 2014;89(1):88–96.
 23. Prus E , Peled T , Fibach E . The effect of tetraethylenepentamine, a synthetic copper chelating polyamine, on expression of CD34 and CD38 antigens on normal and leukemic hematopoietic cells. *Leuk Lymphoma* 2004;45(3):583–9.
 24. Franceschi C , Bonafè M , Valensin S , Olivieri F , De Luca M , Ottaviani E , et al. Inflamm-aging. An evolutionary perspective on immunosenescence. *Ann N Y Acad Sci*. 2000;908:244–54.
 25. Macciò A , Madeddu C . Management of anemia of inflammation in the elderly. *Anemia*. 2012;2012:563251.
 26. Libregts SF , Gutiérrez L , de Bruin AM , Wensveen FM , Papadopoulos P , van Ijcken W , et al. Chronic IFN- γ production in mice induces anemia by reducing erythrocyte life span and inhibiting erythropoiesis through an IRF-1/PU.1 axis. *Blood*. 2011;118(9):2578–88.
 27. Gluba-Brzózka A , Franczyk B , Olszewski R , Rysz J . The influence of inflammation on anemia in CKD patients. *Int J Mol Sci*. 2020;21(3):725.
 28. Yiannikourides A , Latunde-Dada GO . A short review of iron metabolism and pathophysiology of iron disorders. *Medicines (Basel)*. 2019;6(3):85.
 29. Bianchi VE. Anemia in the elderly population. *J Hematol*. 2014;3:95–106.
 30. Ershler WB , Sheng S , McKelvey J , Artz AS , Denduluri N , Tecson J , et al. Serum erythropoietin and aging: a longitudinal analysis. *J Am Geriatr Soc*. 2005;53(8):1360–