

Anaemia in the Elderly -A Clinicopathological Perspective

Dr Srikanth.N.Md¹, Dr Shubha Sangeetha R Md, DNB².

¹-Associate professor, General Medicine, M.S.Ramaiah Medical College and Hospital

²-Assistant professor, Department of Pathology

Abstract:

Introduction: Anemia is the most frequently encountered hematological problem in the elderly, requiring early identification and treatment since it is an important sign pointing toward serious yet treatable conditions. In this study we analyzed the distribution and characterization of anemia in elderly w.r.t age and sex and to determine the possible underlying etiology.

Patients and methods: 100 elderly individuals above 60 years of age diagnosed with anemia in M.S.Ramaiah Medical College/ Hospital were studied. Basic hematological investigations comprising of Hb, Hct, TC, DC, Platelets, RDW, Reticulocyte count and supporting investigations including RFT, LFT, TFT, Iron study, VitB12, Folate, FBS, PPBS, and HbA1c were done to determine the possible etiology. Based on the peripheral blood smear finding and RDW correlation, different types of anemia were categorized.

Results: Out of 100 cases of anemia in the elderly: Age distribution-68% were between 60-70 yrs, 32% more than 70 yrs. 58% were males and 42% were females. The categorization of anemia was as follows:- 48% of cases-normocytic normochromic (NNBP), 38% - microcytic hypochromic (MHBP), 8% - macrocytic and 6% - pancytopenia. The most common possible etiologies derived from our study were: NNBP- Renal Insufficiency secondary to Diabetes, MHBP- Iron deficiency and G.I. causes, Macrocytic Blood Picture- Vit B12 deficiency and Pancytopenia- VitB12 deficiency, Aplastic anemia.

Conclusion: Identifying and categorising anemia is essential to direct the investigation for deriving the etiology for targeted treatment and improving the quality of life in the elderly.

Keywords: anemia, elderly, categorization, etiology.

I. Introduction

Anemia 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 anemia is one such problem¹.

Anemia is often defined in terms of the WHO criteria, established in 1968². The WHO definition of anaemia is a Haemoglobin (Hb) concentration <130 g/L in men and <120 g/L in women³ and this is by far the most widely accepted.

Haematocrit (Hct) levels are sometimes used to define anaemia. Hct 39% for men and 36% for women are alternative WHO criteria for defining anaemia.²

The prevalence of anemia has been found to range from 8 to 44%.⁴

NHANES-III of WHO study revealed prevalence of anaemia as 11% of men and 10.2% of women aged 65 years and older⁵.

This prospective observational study was conducted to study the distribution of anemia in the elderly with reference to age, sex and classify anemia's and assess the frequency of anemia types in the elderly and to determine the possible underlying etiologies for profiling targeted treatment.

Setting: A tertiary hospital based study.

II. Materials And Method

This prospective observational study was conducted in M.S.Ramaiah Medical College/Hospital. 100 cases of elderly individuals above 60 years of age, fulfilling the WHO criteria of anemia [Hb < 13g/dl in males and Hb < 12 g/dl in females⁸ were studied. In all these cases a detailed medical history including diet, medications and habits were recorded. Distribution of anemia with reference to age and sex were studied.

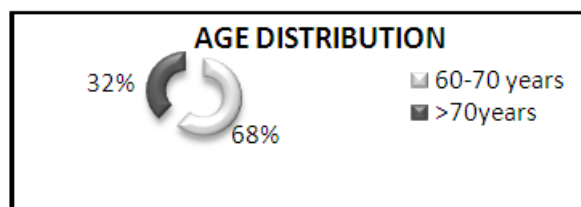
Based on peripheral blood smear findings, different types of anemia were categorized. Basic hematological investigations comprising of Hb, Hct, RDW, MCV, MCH, MCHC, TC, DC, platelets and retic count were correlated with peripheral blood smear and studied.

Supporting investigations including S.Ferritin, serum Vit B₁₂ and Folate assays, RFTs, LFTs, TFTs stool for occult blood and HbA_{1c} were done pertaining to the type of anemia detected on PBS and results were analysed to determine the underlying possible etiology.

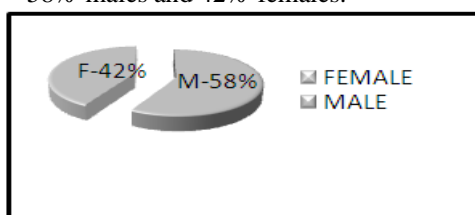
Bone marrow aspiration and biopsy were done in select cases when indicated.

III. Results

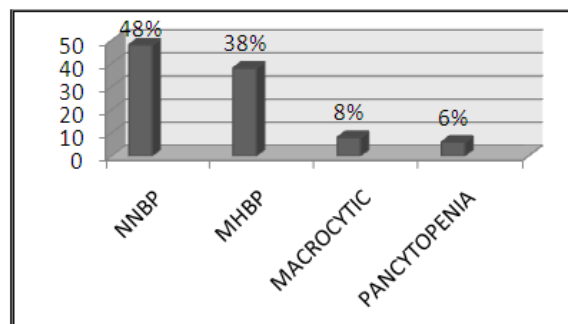
Patient's age range : 60-88 yrs
 Mean age : 73.5 yrs
 Age distribution : 68% in the age group of 60-70yrs
 28% in the age group of 71-80yrs
 4% in the age group of 81-88yrs



Sex : 58%-males and 42%-females.



Anemia categorised on PBS:



NNBP: 48 patients out of 100 patients had Normocytic normochromic blood picture. Renal insufficiency was the most common underlying etiology identified. 30/48 patients having deranged RFT's 23/30 CRF patients were diabetics with 16 patients on regular hemodialysis. PBS of CRF patients showed significant burr cells. Hypothyroidism was detected as an underlying etiology in 4/48 patients. A NNBP associated with a low reticulocyte count was the initial clue to coexistent renal or endocrine disease. Stool for occult blood was positive in 3/48 patients. 2/48 patients had chronic inflammatory disorder. 1 had osteoarthritis and 1 had tuberculosis. 1/48 patient was diagnosed with multiple myeloma.

MHBP: 38 patients out of 100 patients had MHBP. This was based on MCV < 80 fL and PBS findings on which majority of RBCs were microcytic (smaller in size when compared to the nucleus of a small lymphocyte) and hypochromic when the central pallor was > 2/3rd of the RBC diameter. 12/36 patients were positive for occult blood in stool. GI endoscopy done in 10 patients revealed superficial gastric erosions in 5 cases, peptic ulcers in 2 cases, malignant growths (adenocarcinoma stomach-1 case, adenocarcinoma in colon- 1 case) and 1 case of adenomatous polyp.

S. Ferritin levels were estimated in all patients. 15/36 patients had S. Ferritin values < 20ng/ml. Iron deficiency anemia was the most common underlying etiology detected, followed by Anemia of chronic disease. Macrocytic blood picture :8/100 patients had macrocytic anemia. This was based on MVC>100 fl and PBS showing predominantly macrocytosis when compared with nucleus of small lymphocyte, macro ovalocytes and hypersegmented neutrophils. 4/8 patients had VitB₁₂ deficiency confirmed by serum VitB₁₂ assays. Bone marrow examination were done in select cases. Vit B₁₂ deficiencies was considered when serum Vit B₁₂

was <150 pmol/L. 2/8 patients had myelodysplasia as confirmed by bone marrow examination. 2/8 patients had deranged LFTs with history of alcoholism in 1 patient and the other patient on antiretroviral drug therapy. **Pancytopenia** : 6/100 patients had pancytopenia with Hb < 10g/dl. TC <4,000/ μ l and platelets <1.5 Lakh/ mm^3 . The underlying etiologies identified were 3 cases of Vit B₁₂ deficiency, 2 cases of aplastic anaemia and 1 case of chemotherapy induced pancytopenia in a patient diagnosed with ovarian malignancy with metastases.

IV. Discussion

Anemia as defined by WHO criteria, is common in older people, affecting 1 in every 7 or 8 over 60 years, living in the community¹.

The WHO criteria of Hb < 130g/L for men and <120g/L for women was by far the most commonly used to define anemia in the literature and also because they do appear relevant, correlating with clinical outcomes¹.

The mean age distribution of anemia in elderly in our study was 73.5 years. 68% of elderly with anemia were between the age group of 60-70 years and 32% were between the age group of 70-88 years.

In a study done by Amit Bhasin et al, the mean age was found to be 70.51 years⁶.

In our study prevalence of anemia was higher in males (58%) than females (42%).

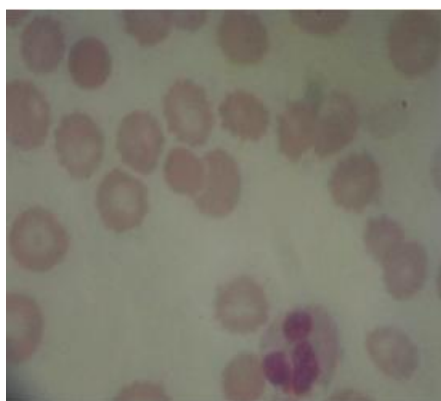
Hemoglobin concentration though slightly, was age related, a cross sectional estimated study revealed a mean yearly decline to be more pronounced in men than in women (-0.08 and -0.05 g/dl respectively P <0.0001)⁷.

When anemia is diagnosed, initial information to be obtained includes a detailed clinical history and basic investigations like the hemoglobin, hematocrit, red cell indices, total leukocyte count, platelet counts, peripheral blood film, and the reticulocyte count. Multiple etiologies for anemia may exist in the same individual, so careful description and analysis of the anemia is important⁸.

NNA was the most common type of anemia categorised from this study (48%). The peripheral blood smear of many patients revealed presence of burr cells and correlated with deranged RFTs. Renal insufficiency secondary to diabetes was the most common etiology identified.

In patients with CKD, NNBP mainly develops from decreased renal synthesis of erythropoietin. The anemia becomes more severe as the GFR progressively decreases. No reticulocyte response occurs, RBC survival is decreased and there is an associated increased bleeding tendency due to uremia induced platelet dysfunction. Other causes of anemia in CKD includes the presence of uremic inhibitors (eg parathyroid hormone, inflammatory cytokines) and reduced half life of circulating blood cells⁹, deficiencies of folate and VitB₁₂.

In patients with CRF, patients with diabetes are at a greater risk of developing anemia, earlier in the course of their disease associated with inappropriately low levels of erythropoietin, comparing with patient with similar eGFR and erythropoietin levels, those with type 2 diabetes are generally more anemic¹⁰.



Anemia might increase risk for ESRD in diabetic nephropathy patients. Anemia could aggravate fibrosis in the failing kidney by causing renal tissue hypoxia¹¹.

Renal hypoxia is known to stimulate cytokines such as hypoxia inducing factor-1 which contributes to renal scarring¹².

Anemia is an adverse indicator for progression of CKD. Correcting anemia is considered an important part of slowing or even stopping the progression of CKD¹³. 38/100 patients revealed microcytic hypochromic blood picture on peripheral blood smear and MCV < 80 fL, hence were categorised to have microcytic hypochromic anemia.

Iron deficiency is the major underlying etiology identified.

Numerous age related parameters and underlying disease influence the nutritional status of elderly patients. The decrease in lean body mass and basal metabolic rate with age may also contribute to the development of a physiological anorexia of ageing¹⁴.

Various concomitants of old age like physical disabilities eg restricted mobility of upper extremity, chewing problems, swallowing disorders result in difficulties for preparing meals and eating¹⁵. A high prevalence of anemia has been observed in hospitalized or institutionalized older individuals^{16,17}.

Inflammation and chronic blood loss, predominantly from the gastrointestinal tract, are frequent etiologies of anemia in the elderly, especially in developed countries^{18,19}.

The impairment of iron metabolism secondary to inflammation shares many laboratory abnormalities with iron deficiency such as a low mcv, serum iron level and transferrin saturation²⁰. However, in contrast to iron deficiency, serum ferritin is increased in inflammatory disease²¹.



Peripheral blood smear correlated with red cell indices, serum ferritin levels and sometimes supplemented by markers of inflammation, that are interpreted in the context of clinical features, permit the diagnosis of majority of cases²².

8/100 cases were categorized as having macrocytic anemia, based on PBS findings and MCV >100fl. The most common underlying etiology identified was VitB₁₂ deficiency.

Many elderly subjects have a decreased gastric production of acid, due to the increase in the prevalence of atrophic gastritis. In this condition there is low vitamin B₁₂ absorption because the protein bound vitamin is not dissociated and therefore it will not bind to the intrinsic factor. Alternatively the loss of acid can increase stomach and small intestine bacterial overgrowth which can uptake or bind the Vit B₁₂ and thus limit vitamin B₁₂ bioavailability^{23,24}.

The high prevalence of folate deficiency found in elderly subjects may be explained by a reduced consumption of vegetables and fresh fruits and by the custom of overcooking foods which destroys this heat labile vitamin and also aged subjects have defective folate polyglutamate absorption. A reduction in gastric acid production is associated with a decreased absorption of folate²⁵.

Moreover folate metabolism may be adversely affected by alcohol ingestion. Unsuspected problem of alcoholism in the elderly is being more frequently recognized as a contributing factor.

In alcoholism the mcv is usually reported to range between 100 to 110 fl²⁷.

Ethanol appears to have a direct toxic effect on marrow erythroid precursors. As the life span of erythrocyte is 120 days it may take 3-4 months for mcv to return to normal following abstinence from alcohol²⁷.

It is reported that an mcv >115fl, increased RDW, macroovalocytes and hypersegmented neutrophils suggest a megaloblastic disorder²⁸.

Nonmegaloblastic conditions display uniformly round macrocytes and normal RDW²⁹. Round macrocytes are commonly seen in alcoholism, drug induced macrocytosis and round, target appearing macrocytes are characteristic of liver disease.

Reverse transcriptase inhibitors, anticonvulsants and chemotherapeutic agents were most common drugs inducing macrocytosis³⁰. 6/100 patients were diagnosed to have pancytopenia based on presence of anemia, leucopenia (TLC < 4000/ μ L) and thrombocytopenia (platelet count < 1.5 lakh/mm³)

An elevated reticulocyte count in this setting would suggest peripheral destruction of cells, as might occur with splenomegaly of any etiology. More often the reticulocyte count is low in pancytopenia, may be secondary to a nutritional deficiency of Vit B₁₂ and folate. Aplastic anemia though uncommon increases in frequency with age.

Most often pancytopenia is the result of anticancer chemotherapy, HIV infection, hypersplenism and bone marrow infiltration or failure. Careful examination of blood film is important if the reason for pancytopenia is not apparent from the clinical history. If this does not reveal the cause, bone marrow aspiration and trephine biopsy may be needed³².

Impact of Anemia on elderly:

Older people with anemia suffered higher mortality (57%) than those without anemia (39%) when followed up for almost 12 years³³.

Anemia is also associated with increased risk of falls and impaired muscle strength³⁴, executive function impairment³⁵ and dementia³⁶, hospital admissions and longer hospital stay³⁷ and tremendously induces financial and economical constraints.

V. Conclusion

Anemia is a common and frequently under diagnosed clinical condition in the elderly associated with increased morbidity and mortality and hence requires strict evaluation for detecting potentially treatable underlying etiologies for targeted treatment. Specific findings in the PBS and a good clinical correlation can tailor or truncate further testing, eliminating unnecessary investigations. In some cases hospitalization can be minimized or eliminated and financial burdens on elderly can be curtailed.

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Author contributions

Dr. Srikanth. N, M D General Medicine: Conception, clinical data collection and conduction of the study.

Dr. R. Shubha Sangeetha, MD, DNB Pathology: Interpretation and analysis of laboratory parameters, compilation and paper work.