

**ANEMIA IN ELDERLY: AN AGING PROCESS OR A DISEASE MARKER?****^{1*} DR.C.A.ARATHI, ²DR.N. PRABHUDEVA.N AND ³DR. ARUNDHATHI.S**¹*Prof, Dept of Pathology Sri Siddhartha Medical College and Research Centre Tumkur-572107*²*Associate Prof, Dept of Internal Medicine Sri Siddhartha Medical College and Research Centre Tumkur-572107*³*Assistant Prof, Dept of Pathology Sri Siddhartha Medical College and Research Centre Tumkur-572107***ABSTRACT**

Background: Population based surveys have renewed the debate and have referred to the high prevalence of anemia among elderly people as a “public health crisis”. Anemia of any degree is recognized as a significant independent contributor to morbidity, mortality, and frailty in elderly patients. Efforts to understand anemia in elderly has become a major target of research interest. About one third of them have anemia secondary to nutritional deficiency, one third due to chronic inflammation or chronic renal disease, and one third have unexplained anemia. Aim: To study the morphological types and etiologies of anemias in elderly. Material and methods: 100 patients (either sex, >60yrs) were selected, clinical data and various laboratory investigations, complete hemogram, reticulocyte count, blood urea nitrogen, creatinine and serum ferritin were done for all and special investigations like bone marrow study, endoscopy, ultrasound examinations etc were done wherever required. Based on history, clinical evaluation and the laboratory investigations, the anemias were morphologically and aetiologically classified. Results: Majority of the patients had hemoglobin levels in the range of 9.8 to 11.4gm%. Anemia was morphologically typed based on the peripheral smear findings and complete blood counts, into normocytic(42%), microcytic(28%), macrocytic(19%), and pancytopenia(11%). Majority of the cases, had anemia of chronic diseases(36%) followed by anemia of unknown etiology(24%). 17% included both hematological and non-hematological malignant cases. Conclusion: Until further data are available, anemia in the elderly should be evaluated and remediable causes treated, but the anemia itself should not be treated unless the patient is severely symptomatic or in danger of needing a transfusion.

KEY WORDS: public health crisis, comorbidity, unexplained anemias,**DR.C.A.ARATHI**Prof, Dept of Pathology Sri Siddhartha Medical College
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INTRODUCTION

Hematology researchers have had a long standing interest in the pathophysiology and clinical implications of anemia as associated with aging. The third National Health and Nutrition Examination Study (NHANES III) highlighted the importance of this issue with respect to the public health. It indicated that even when "mild" anemia is present, it either causes and/or is associated with both significant functional impairment and, perhaps, increased patient mortality¹. The World Health Organisation definition of anemia is hemoglobin level less than 13 g per dL in men and less than 12 g per dL in women. Using World Health Organization criteria for anemia, the prevalence is found to range from 8 to 44 percent, with the highest prevalence in men 85 years of age and older². Population based studies in Great Britain have reported prevalence ranging from 5% to 25%. Despite the high prevalence of anemia in the elderly and the increasing size of the geriatric population, only few studies have examined the effects of anemia on elderly patients³. The prevalence increases with age, approaching 50 percent in chronically ill patients living in nursing homes. About one third of them have anemia secondary to nutritional deficiency, one third due to chronic inflammation or chronic renal disease, and one third have unexplained anemia. Nutritional anemia can be effectively treated with vitamin or iron replacement. Iron deficiency anemia often is caused by gastrointestinal bleeding and requires further investigation in most patient. Anemia of chronic inflammation or chronic renal disease may respond to the treatment of underlying disease and selective use of erythropoiesis –stimulating agents. The treatment of unexplained anemia is difficult, and there is little evidence that treatment decreases morbidity and mortality or improves quality of life. Anemia can be occasionally caused by less common causes such as malignancy or myelodysplastic syndrome⁴. We have made an attempt to study the morphological and etiological causes of anemia of geriatric age group in patients (>60yrs of age) who visited our institution.

PATIENTS AND METHODS

An observational study was carried out on a cohort of patients aged 60 years and above (either sex) visiting our institution, Sri Siddhartha Medical College and Research Centre, Tumkur. A total of 100 patients were studied. The patient selection was random and non consecutive. The study was approved by Institutional review board. With the informed consent, the present study was carried out from departments of Pathology and Internal medicine. Patients (either sex) with hemoglobin <12 and <13gm% for females and males respectively (WHO criteria) were included in the study. With informed consent, an observational cohort study was carried in 100 patients aged 60yrs and above. A detailed history, clinical examination and laboratory investigations were done accordingly. The following hematological investigations were carried out for all patients- complete haemogram including RBC indices and peripheral smear examination. Retic count, blood urea nitrogen, serum creatinine and serum ferritin were carried out for all patients. Investigations like, bone marrow study, vitamin B12 assay, erythropoietin levels, ultrasonography, electrophoresis, fine needle aspiration, and GI endoscopy and histopathology, were done depending upon the suspected etiologies. Stool occult blood was done for all microcytic hypochromic anemias. Microcytic anemia was diagnosed when MCV is below 80fl, normocytic as MCV between 81 and 100fl, and macrocytic anemia by an MCV above 100fl.⁵ Based on history, clinical evaluation and the laboratory investigations, the anemias were morphologically and aetiologically classified.

RESULTS

Age of the patients ranged from 60 to 94yrs in our study population. The mean age was 77years. High number of patients were seen in the 6th decade. 68% were male and 32% were female patients.(Fig 1) The clinical symptoms of anemia depended on the severity, fatigue and generalised weakness being the commonest. Majority of the patients

had hemoglobin levels in the range of 9.8 to 11.4gm%. Three cases presented with hematuria(bladder carcinoma) , three presented with generalised lymphadenopathy and splenomegaly(CLL/SLL) and one patient had anemia associated with bony tenderness(multiple myeloma). Five patients had loss of appetite and weight(GI malignancy). Anemia was morphologically

typed based on the peripheral smear findings and complete blood counts, into normocytic(42%), microcytic(28%), macrocytic(19%), and pancytopenia(11%).(Fig II) Majority of the cases, had anemia of chronic diseases(36%) followed by anemia of unknown etiology(24%). 17% included both hematological and non-hematological malignant cases(Fig III).

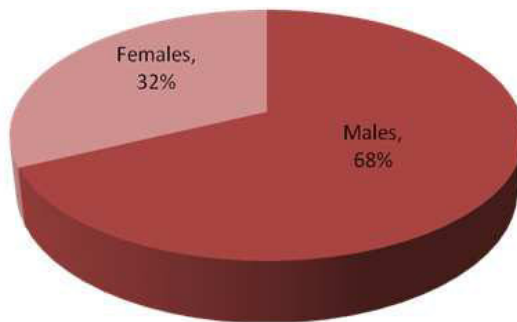


Figure I
SEX DISTRIBUTION IN 100 CASES OF ANEMIAS.

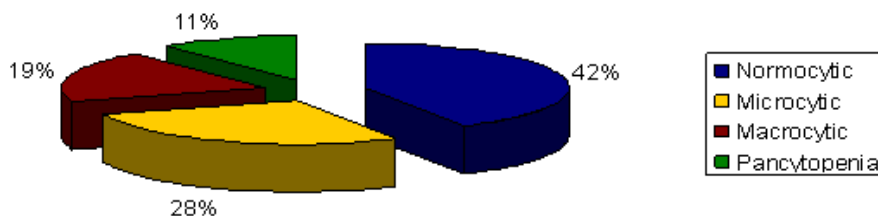


Figure II
MORPHOLOGICAL PATTERNS OF ANEMIAS.

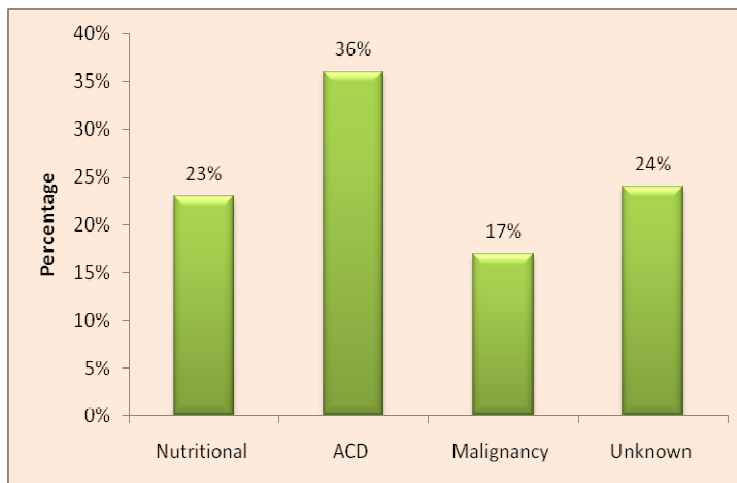


Figure III
PERCENTAGE OF ANEMIAS OF VARIOUS CAUSES.

Normocytic anemias: (Fig VI)

Majority (42) of the cases had normocytic anemias. (3 cases of hypoplastic marrow) 17 cases had no underlying disease. 11 had type 2 diabetes of long duration. They had no identifiable underlying aetiology. Interestingly 6 cases of chronic obstructive pulmonary disease had moderate degree of anemia. 4 cases of pulmonary tuberculosis and 3 cases of hypoplastic marrow had anemia. All 3

patients of hypoplastic marrow were in 6th decade and had no history of any chronic disease, medication or organomegaly. Peripheral smears showed moderate degree of anemia with pancytopenia, and marrow had reduced 3 cell lineages with relative increase in lymphocytes. 3 cases of chronic lymphocytic leukemia and 1 case of multiple myeloma were reported.

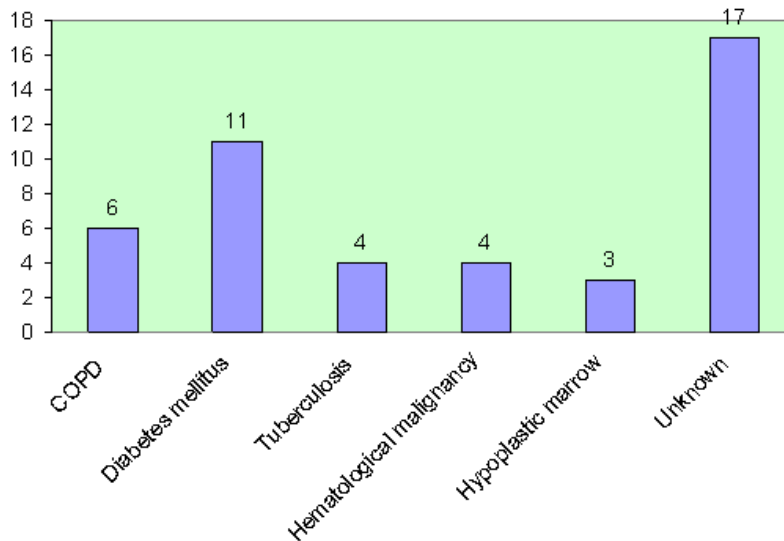


Figure VI
CAUSES OF NORMOCYTIC ANEMIAS.

Microcytic anemias: (Fig V)

Serum ferritin levels and stool for occult blood was carried out in all 28 cases of microcytic anemias, 12 had nutritional anemia (7 females and 5 males). Serum ferritin levels were below low normal reference range(<20ng/ml). Eight patients had

malignant tumors (5-gastro intestinal and 3-bladder) with low serum iron levels. 11cases were positive for stool occult blood, out of which 3 had GI malignancy. Anemia of unknown cause were with low erythropoietin levels and renal anemias had normal serum ferritin levels.

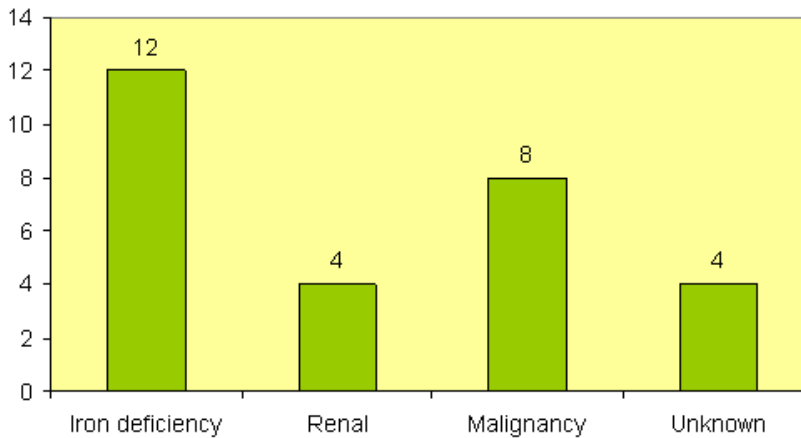


Figure V
CAUSES OF MICROCYTIC ANEMIAS.

Macrocytic anemias: (Fig VI)

Among macrocytic anemias, vit B12 deficiency was the commonest cause. The hemoglobin levels in these patients ranged from 5gm% to 9gm%. There was a increase retic response, days after initiation of therapy. All hypothyroidism patients were females. Two cases of chronic hepatitis(HBV) and 1 case of cirrhosis were reported with moderate degree of anemia. Five cases of

MDS were diagnosed based on bone marrow features with tri-lineage dysplasia. All 5 were in 6th decade. 11 (100) presented with pancytopenia. 5(MDS), 2(vit B12 deficiency), and 3 (hypoplastic marrow) and 1 case of multiple myeloma. Anemia of unknown origin constituted 24% of the cases, where no etiology could be identified. The EPO levels in 17(24) of the cases were low.

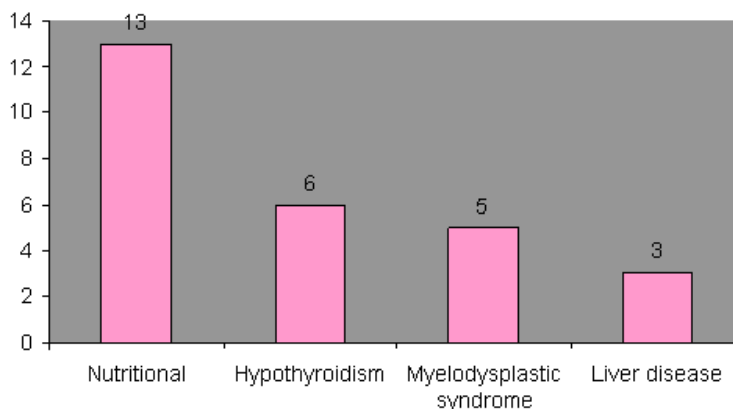


Figure VI
CAUSES OF MACROCYTIC ANEMIAS.

Hematological and non-hematological malignancy: (Fig VII & Fig VIII)

17 cases were found to have malignant lesions. Five cases of Myelodysplastic syndromes were reported. Age ranged from 60 to 75yrs. All were male patients. Three cases were reported as CLL /SLL, who presented with generalized lymphadenopathy. One case of multiple myeloma was diagnosed on bone marrow

features and confirmed by serum electrophoresis. Three cases of adenocarcinoma colon were diagnosed on histopathological features and one case of gastric adenocarcinoma was detected on endoscopy biopsy. 3 patients who presented with hematuria, on evaluation had urothelial carcinoma. All three cases of bladder tumors were in 7th decade.

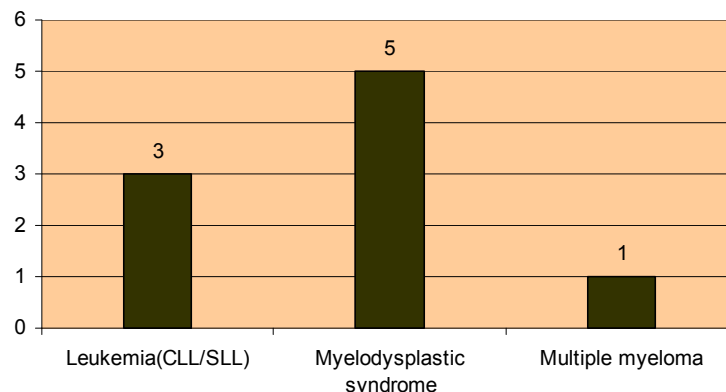


Figure VII
HEMATOLOGICAL MALIGNANCIES.

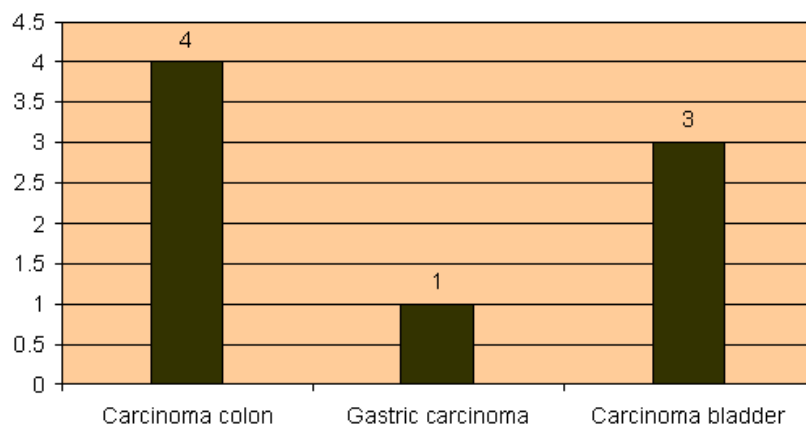


Figure VIII
NON-HEMATOLOGICAL MALIGNANCIES.

DISCUSSION

Anemia is a public health problem affecting some 164 million elderly people worldwide⁶. Population based surveys have renewed the debate and have referred to the high prevalence of anemia among elderly people as a “public health crisis”. Anemia of any degree is recognized as a significant independent contributor to morbidity, mortality, and frailty in elderly patients. Efforts to understand anemia in elderly has become a major target of research interest⁷. Although there is a paradoxical feedback in renal production of erythropoietin, since the levels of this hormone actually increase over time, it has also been reported that the erythroid marrow may become less sensitive to erythropoietin stimulation, a key factor contributing along with possible nutritional deficits and co morbidities to the development of anemia in the elderly⁸. The causes of anemia in the older adult were evaluated in a study of the non institutionalized United States population in the third National Health and Nutrition Examination Survey (NHANES III). NHANES-III study has revealed prevalence of anemia in 11% of men and 10.2% of women aged 65 years and older⁹. In another study, Ferrucci and colleagues reported that 8% of non-anemic older adults subsequently went on to develop anemia at 3-year follow-up and showed that low levels of total and bioavailable testosterone significantly predicted anemia onset. A similar 3-year estimate of 7% was observed in a relatively small cohort study of older Koreans¹⁰.

Saurabh R Shrivastava et al reported 78.05% of normocytic anemias being the commonest, followed by microcytic hypochromic 11.6%, macrocytic 6.02% and dimorphic 4.24 %¹¹. We reported 42% of normocytic anemias followed by 28% of microcytic anemias. In the absence of any hemorrhage, microcytic anemia is sometime related to diet, but is usually a result of occult gastrointestinal bleeding. Common causes include NSAID use, colonic cancer or polyp, gastric cancer, angiodysplasia and inflammatory bowel disease¹². The serum ferritin level is the most effective way to diagnose iron deficiency anemia. When serum ferritin is <20 ng/ml, iron deficiency is virtually certain¹³. Endoscopic evaluation in iron deficiency anemia in elderly is likely to find an underlying abnormality. In a study of 100 consecutive older patients with iron deficiency anemia¹⁴. Rocky and Cello found 16% of patients with underlying colon cancer or premalignant polyps¹⁵. In our series, 4% of GI malignancy and 3% of urothelial carcinoma were reported in patients with microcytic anemias. One study reported 3.35% cases of colonic carcinoma in patients with IDA⁵. Among macrocytic anemias, vit B12 deficiency was the commonest cause. Catastrophic neurologic complications from B 12 deficiency may occur despite modest anemia and are readily prevented by timely diagnosis and treatment with supplementation¹⁴. Anemia of inflammation has historically been termed the “anemia of chronic disease” and is most commonly seen in association with infection, rheumatologic disorders, malignancy, and other chronic illnesses.

However, distinguishing anemia of chronic inflammation from iron deficiency anemia is particularly challenging in older adults because of the comorbid effects of gastrointestinal bleeding as well as the effects of medications¹⁰. Among the anemias of chronic diseases, the highest number of cases reported were type 2 diabetes mellitus. Diabetes mellitus is another potential confounder, because with any degree of renal impairment, erythropoietin production is reduced more in those with diabetes mellitus. It is likely that some proportion of unexplained anemia cases are caused by myelodysplastic syndrome (MDS), another common hematologic condition in older adults. Guralnik et al. liberally estimated that up to 17.2% of unexplained anemia cases (5.8% of all anemia cases) may be attributed to MDS by examining the co-occurrence of neutropenia, thrombocytopenia, or macrocytosis with unexplained anemia¹⁰. Population based studies have demonstrated evidence that vit D deficiency may be a previously unrecognized contributor to the development of anemia and is particularly prevalent among those with anemia of inflammation⁷. However we have not assessed vit D levels in our study. The large number of cases in our series who had anemia of chronic illness was diabetes mellitus. The pathophysiology of unexplained anemia in elderly patients is poorly understood, and it remains primarily a diagnosis of exclusion. It is postulated that overexpression of proinflammatory cytokines

is an important determinant of UA and they induce anemia by suppression of erythroid colony formation on one hand and impairment of iron utilization on the other⁷. Low EPO levels have been associated with unexplained anemias in elderly. This reduced EPO response suggests progressive EPO resistance of the hemopoietic stem cell in the face of aging⁷. In our series, we reported 24% of unexplained anemias compared to NHANES III who reported 34% of unexplained anemias¹. Until further data are available, anemia in the elderly should be evaluated and remediable causes treated, but the anemia itself should not be treated unless the patient is severely symptomatic or in danger of needing a transfusion. Anemia can be a marker for more severe disease or an indicator of lower likelihood to respond to current therapies¹⁶.

CONCLUSION

Future research is needed to define the optimal hemoglobin levels for health, to refine diagnostic testing to sort out the etiology of the unexplained anemias, and to evaluate rigorously therapies designed to augment erythropoiesis. All iron deficiency anemias in elderly should be looked for causes like gastrointestinal bleeding. MDS has to be ruled out in cases of unexplained anemias in elderly.

Conflicts of Interest

We have no financial interests related to the material in the manuscript.

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