Study of Anaemia in the Hospitalised Elderly in a Rural Setup

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ABSTRACT:

Aim

To Study the etiology of anemia in elderly population.

Materials and methods: All elderly patients more than 60 years of age admitted to ABBRH hospital during the period August 1 2003 to January 15 2005 presenting with anemia (hemoglobin less than 10 gm/dl) were included in the study and their full work up was done.

Results

The maximum number of patients were in the age group 60 – 64 years and there was no significant difference in the mean haemoglobin levels as age increases (p=0.3348). The mean haemoglobin in males was 6.44±1.68 gm% and in females was 6.28±1.98 gm%. Morphologically, a total of 53 patients (24 males and 29 females) had microcytic anaemia, 27 (17 males and 10 females) had normocytic anaemia and 10(8 males and 2 females) had macrocytic anaemia. The present study found 49% microcytic, 34.7% normocytic and 16.3% macrocytic in males as compared to 70.7% microcytic, 24.4% normocytic and 4.9% macrocytic in females. ACD is the most common type of anaemia in elderly patients seen in this study. In 46.6%of the cases possible cause of anaemia could be found. The remaining cases could be nutritional in origin, due to aging or due to undetermined causes. Cause of anaemia was found in 37% of the patients in the IDA group and in 56% of the patients in ACD group. Tuberculosis and chronic renal insufficiency were the common causes found in ACD. Marrow disorders and leukaemia/lymphoma were found to be the cause in only 4.4% of the cases.

Conclusion:

Most of the patients (53) had microcytic anaemias, while the next common was normocytic anaemias (27). In our study, microcytic anaemias were more common in females. Macrocytic anaemias were more severe in our study.

Keywords: Anemia, elderly, etiology

INTRODUCTION:

Advances in medical science have resulted in a significant rise in elderly population. According to estimates in the next 30 years the number of older persons will nearly quadruple growing from about 600 million to almost 2 billion people. Today 1 in every 10 is 60 years and older. By 2050, 1 out of every 5 will be an older person and by 2150 one third of the people in the world are expected to be 60 years of age or older.[01]

In India expectation of life at birth for males and females has increased more in recent years. In India it is projected to be 67 years in 2011-16 for males and 69 years for females. Projection beyond 2016 made by United Nations has indicated that 21% of Indian population would be 60+ by 2050 which was 6.8% in 1991.[02]

Anaemia is common in the elderly and its prevalence increases with age.[03] Using the World Health Organisation criteria for anaemia (haemoglobin of less than 12g/dl [120g/L] in women and less than 13 g/dl [130g/L] in men) the prevalence of anemia have shown an incidence ranging from 6% to 30% for men and 10% to 22% for women. There is often the impression that there is anaemia of senescence and that in the older patient, a mild anaemia especially is likely to reflect a physiological rather than pathological process. Consonant with this belief, suggestions have also been made that evaluation in the elderly should only begin when the anaemia when the anaemia is at least moderate (less than 10g/dl), since workup of mild anaemia may produce a poor yield of identifiable causes. Conversely, others have stated that anaemia should always be regarded as being pathological and hence evaluated so

as not to miss any underlying treatable conditions especially in their early stages.[04]

Although studies have been made in other countries, unfortunately there have been few domestic studies on the incidence and etiology of anaemia in the hospitalized elderly in a rural setup. This prospective study was undertaken to present some Indian data on the subject.

AIMS AND OBJECTIVES:
To Study the etiology of anemia in elderly population.

MATERIAL AND METHODS:
Acharya Vinoba Bhave Rural Hospital is a 750-bedded hospital situated at Sawangi (Meghe), a village in Wardha district of the state of Maharashtra, India. The patients admitted to the Medicine ward in this hospital from August 1, 2003 to January 15,2005 were included in this study. For patients admitted more than once during the study period only the first admission was considered. The patients in this ward (all 60 years and above) generally came from the lower socio-economic strata. Only those subjects with haemoglobin of less than 10g/dl were fully investigated (including history, general and systemic examination and appropriate laboratory evaluation). These included patients admitted with other disorders not directly resulting in anaemia (e.g. myocardial infarction, hypertension, diabetes, asthma). Patients with an obvious history of blood loss (eg: bleeding piles), those with an established cause (e.g. diagnosed CRF/malignancy) and those with acute life threatening illnesses were excluded. Of a total of 110 subjects 20 were excluded (12 had obvious history of blood loss, 3 were known cases of malignancies (2 CLL and 1 Carcinoma cervix), 2 dropped out in the middle of the study, and 3 patients had acute life threatening illnesses.

The anaemic patients were identified (generally based on single readings of the haemoglobin value) and several features were studied such as age and sex distribution, and the underlying diagnosis of the various anaemias. Work up for anaemia included haemoglobin, peripheral smear, Mean Corpuscular Volume (MCV), serum iron, serum total iron binding capacity (TIBC) [Ferrozine method-Span Diagnostics], serum ferritin [ELISA-Merck Labkit], stool for occult blood [Benzidine test], and bone marrow studies including Prussian blue iron staining. Transferrin saturation was calculated as S.Iron/TIBC x 100 (normal: 30% to 50%). An independent observer who was blinded about the details of the patient and other parameters did the grading of the marrow iron smears using the criteria for grading iron stores in squashed marrow fragments.[37]

- Iron deficiency anaemia was diagnosed when the serum ferritin was decreased (normal serum ferritin: 50-200µg/L) or when a decreased serum iron (normal serum iron: 50-150µg/dl) was accompanied by an increased TIBC (normal TIBC: 300-360µg/dl) with the transferrin saturation being less than 10%.
- Anaemia of chronic disease was diagnosed when, The serum ferritin was normal or elevated, or ii) when both the serum iron and TIBC were decreased with the transferrin saturation being in the normal range.
- Macrocytic anaemia was diagnosed by blood and bone marrow picture.[5]

Statistical analysis:
Statistical analysis was performed on the computer using the SPSS version 10.0 & the GraphPad Instat software. Statistical methods employed were

1. Percentages
2. Mean $\pm$ 1S.D calculated for individual groups.
3. Student's unpaired t test for comparing different variables in two groups.
4. Chi^2 test and Fishers exact test for the same.
5. One way analysis of variance (ANOVA) for comparing variables in more than two groups.
6. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), accuracy and likelihood ratio were computed from 2 X 2 contingency table.

$p<0.05$ was considered significant.

RESULTS & DISCUSSION:
Total 90 patients were fully evaluated for cause of anaemia. Of these 49 were males, and 41 were females. The maximum numbers of patients (20 males and 15 females) were in the age group 60-64 years. The mean ($\pm$1 S.D.) age in males was 65.67$\pm$4.69 years and that in females was 64.53$\pm$3.97 years. Age difference was statistically not significant. (p=0.2218). There was no significant difference in the mean haemoglobin levels as age increases (p=0.3348). This is similar to the study by **Matzner et al**[06] who observed that reduction in haemoglobin does not increase linearly with age. But in some other studies (**Hawkins et al,** 1956; **Myers et al,**

1968; **Takkinen**, 1976) a gradual decrease of haemoglobin levels in men and women has been observed beyond the 6th decade of life. **Campbell et al**[07] found no significant change in haemoglobin with age till 80 years.

Hb g%	60-64		65-69		70-74		75-79	
	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE
2.0-4.0	5	5	0	3	2	0	0	0
4.1-6.0	1	5	6	3	4	2	1	1
6.1-8.0	12	3	3	10	5	0	0	0
8.1-10.0	2	2	3	4	4	2	1	1
TOTAL	35		32		19		4	

TABLE No.1: HAEMOGLOBIN AND AGEWISE DISTRIBUTION IN MEN AND WOMEN.

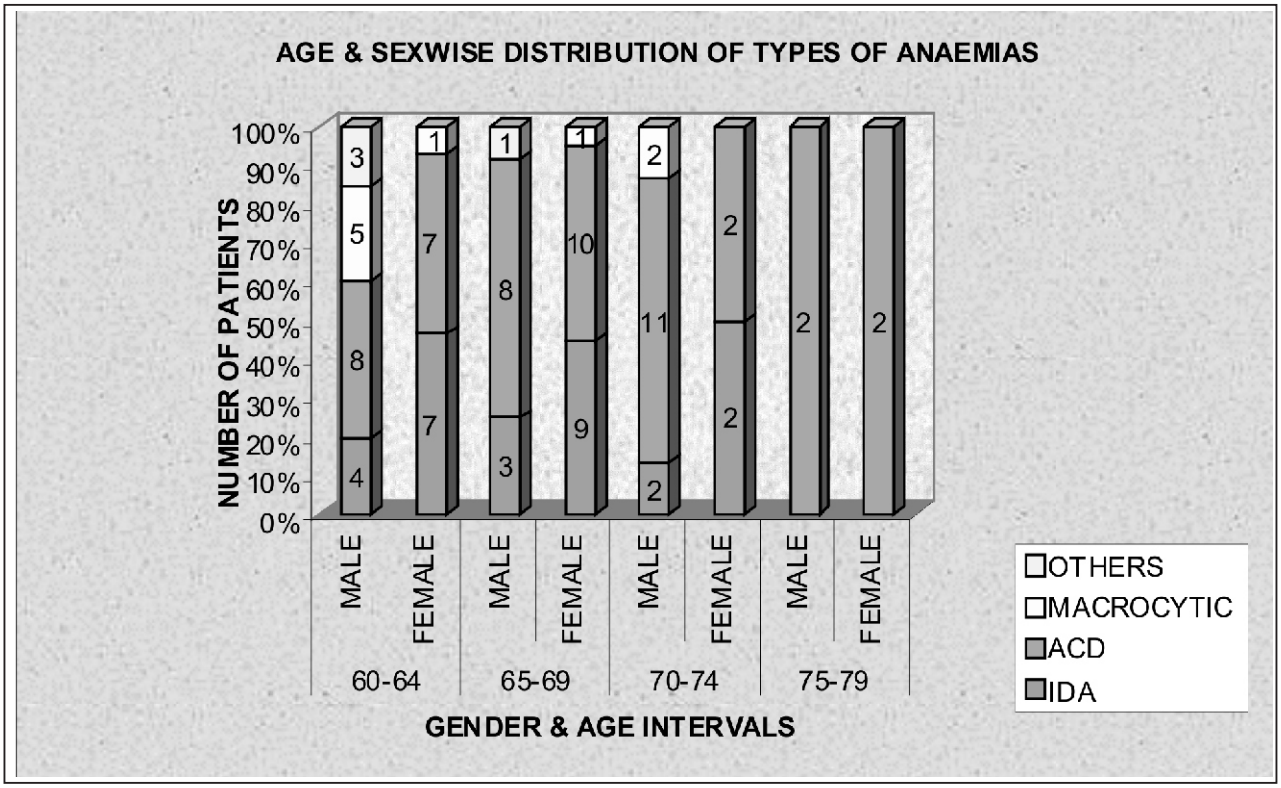
The mean haemoglobin in males was 6.44±1.68 gm% and in females was 6.28±1.98 gm%. The severity of anaemia in either sex was comparable. (p=0.6781). Earlier studies demonstrated lower mean haemoglobin level in women and decreases in haemoglobin levels with age. **Milne and Williamson**[07] found that mean haemoglobin level for men was significantly higher than women. They also found a decrease in haemoglobin levels with increasing age in men but not in women. **Ellwood et al**[07] showed only a small decrease in haemoglobin and PCV levels with increasing age.

Morphologically, a total of 53 patients (24 males and 29 females) had microcytic anaemia, 27 (17 males and 10 females) had normocytic anaemia and 10(8 males and 2 females) had macrocytic anaemia. The present study found 49% microcytic, 34.7% normocytic and 16.3% macrocytic in males as compared to 70.7% microcytic, 24.4% normocytic and 4.9% macrocytic in females. In contrast, **Salive et al**[08] found majority of the patients have normocytic type of anaemia in males (81%) and females (80%). **Izaks GJ et al**[09] in his study also found that majority of the men (91.67%) and women (80.21%) have normocytic type of anaemia. Females had significantly lower MCV (fl) (72.34±16.58) as compared to males (80.38±18.2) in our study (p=0.0325). This is similar to findings of **Ania BJ et al**[10] in a population based study.

Of the 90 patients, only 5 had stool for occult blood positive. Of these 4 had microcytic anaemia and 1 had normocytic anaemia. Of these, 2 had peptic ulcer on upper gastrointestinal endoscopy while one had a growth in the rectal wall on proctoscopy. In 2 patients the cause could not be evaluated. Only 7 patients (3 males and 4 females) had a history of use of incriminating drugs (NSAIDs in all the cases) for intervals ranging from 1 month to 1 year. Of these 3 had microcytic anaemia and normocytic anaemia each while one had macrocytic anaemia. Incriminating drug was associated with stool for occult blood in 3 out of the 7 cases. NSAIDs are a recognized case of gastrointestinal irritation and possible blood loss. Elderly people taking an anti-inflammatory preparation warrant close supervision. There remains a possibility of under reporting of drug use.

Bone marrow iron staining was done in all 90 cases. Grading was done as 0 (absent), 1+, 2+, 3+, 4+ depending upon the quantity of haemosiderin seen in the reticuloendothelial cells. Marrow iron was absent in 22 cases while iron stores were present in 65 cases. 3 slides were inconclusive. Serum Iron was measured in all patients. Normal serum iron level (50-150 µg/dl) was found in 19 (21.34%) patients and low serum iron levels (<50 µg/dl) were found in 70 (78.65%) patients. One female patient had serum iron value more than 150 µg/dl. Of the 70 patients with low serum iron, 48 patients (68%) had microcytic anaemia, 19 patients (27%) had normocytic anaemia and 3 patients (4%) had macrocytic anaemia. The mean serum iron (µg/dl) in patients with IDA is 27.37±4.81, in ACD is 48.39±25.3 and in macrocytic anaemias is 67.25±21.79. Thus it was observed in our study that IDA has the lowest serum iron levels and that the difference in the serum iron levels in various types of anaemias is statistically significant (p<0.0001).

	IDA		ACD		MACROCYTIC		OTHERS	
	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE
Mean Hb (g%)	6.62+1.2	6.06+2.03	6.94+1.34	6.52+1.92	4.31+1.77	5.8+3.11	6.2+2.6	0
	6.24±1.76		6.76±1.62		4.64±1.98		6.2±2.6	



Of the 27 patients with IDA, 24 (88%) had S. Ferritin levels consistent with IDA. In ACD uniformly all 50 patients had normal or above normal S.Ferritin levels. Thus S.Ferritin was able to distinguish between ACD and IDA even though patient had microcytosis and variable iron staining and S.Iron level. S. Ferritin has been a most valuable addition to assessment of iron stores and in the uncomplicated iron deficiency, it is both highly specific and sensitive. Unfortunately numerous influences tend to elevate the serum Ferritin in an older population. It appears to rise with aging but in addition it also rises in acute and chronic inflammatory conditions particularly those affecting the liver[11,12]. Thus if one takes the cutoff level of 15µg/l it remains an extremely specific test (95.38%) for iron deficiency, but its sensitivity in this population remains unacceptably low (50%). **Smieja E J et al**[13] showed that when S. Ferritin level is < 15 µg/dl the likelihood ratio of diagnosing IDA is 51.85.

Majority of the patients with IDA (24 of 27 i.e. 88.89%) had TIBC (>360) consistent with the diagnosis of IDA, 2 had normal while 1 had below normal TIBC. In ACD irrespective of their morphology, TIBC was either normal or less than normal. Only 1 patient had TIBC more than normal in our study. S. Ferritin and TIBC have good correlation with each other in both ACD and IDA. Transferrin saturation correlates well with marrow iron stores, S.Iron, S. Ferritin and S.TIBC in our study. This contrasts with **Thomson WG**[14] who did not find the ratio an adequate gold standard for diagnosing IDA (Sensitivity of 61% and specificity of 86%). Standard textbooks of medicine offer advice on the distinction between iron deficiency and ACD. There are however numerous reasons why in geriatric patients this distinction becomes more difficult. The serum iron level

is not constant and varies considerably throughout the day particularly in relationship to meals. Also, S. Iron is often reduced in malignancies, inflammatory conditions, and in association with myocardial ischemia. It is often elevated following chemotherapy and also immediately following iron supplementation either oral or parenteral[15]. The total iron binding capacity appears to fall with aging, but in addition is affected by factors such as malnutrition and chronic disease, which have a high prevalence in this population. Thus the transferrin saturation ratio, which is a derived index, will suffer from the variation in both its numerator (S.Iron) and denominator (TIBC). A low cutoff of transferrin saturation ratio (10%) is highly suggestive of iron deficiency anaemia[11].

ACD is the most common type of anaemia in elderly patients seen in this study.This finding is consistent with that found by **Joosten et al[16], Matzner et al[06]** and **Campbell et al[07]**, but **Sahadevan et al[17]** found macrocytic anaemia to be the most common among established causes.

We found no significant difference in the mean haemoglobin levels in males and females in IDA, ACD and macrocytic anaemias (p>0.3). However there was a significant difference in the mean haemoglobin between ACD and macrocytic group (p<0.001) and IDA and macrocytic group (p=0.0287). Thus in our study macrocytic anaemias had the lowest haemoglobin levels.

In our study IDA group had significantly low MCV. There is significant difference in the mean MCV of patients with IDA (61.05±7.58) fl and ACD (77.59±10.6) fl (p=<0.0001). Amongst microcytic anaemias also, there is a difference in the mean MCV of patients with IDA (61.05±7.58) fl and ACD (68.43±5.8) fl (p=0.0003). But according to **Carmel R[18]** ACD is typically mild and normocytic, although mild microcytosis (MCV=75-82) may occur. There is 87.5% sensitivity and 77.96% specificity in diagnosing IDA at a MCV cutoff of 60fl the PPV being 51.85% and NPV being 95.83%. The likelihood ratio is 3.971. When the cutoff is raised to 65fl the sensitivity decreased to 73.91% and specificity increased to 80.77% the PPV being 62.96% and NPV being 87.5%. The likelihood ratio is 3.843. There is 80.77% sensitivity and 73.91% specificity in diagnosing ACD at a MCV cutoff of 65fl the PPV being 87.5% and NPV being 62.96%. The likelihood ratio is 3.096. When the cutoff is raised to 70fl the sensitivity increased to 90.24% and specificity decreased to 67.64% the PPV being 77.08% and NPV being 85.18%. The likelihood ratio is 2.789. This is significant as in our study 50% of the patients with ACD were microcytic in morphology which is considered to be the feature of IDA for all practical purposes.

In the present study it is observed that the problem of anaemia in elderly usually peaks at the 7th decade and decreases significantly in the latter half of the 8th decade. Only four patients were in the age group 75-79 years. In the Indian context and in rural population contrary to anaemia in young age that is mostly nutritional, in only 42 out of the 90 cases (46.66%) possible cause of anaemia could be found. Remaining cases were possibly of nutritional origin or could they be due to aging only? It is possible that the fall in haemoglobin that occurs with age represents a direct effect of senescence and may be a normal physiological response to aging. A reduction in lean body mass with decreased oxygen requirements are well known features of aging and may result in a reduction in circulating haemoglobin[19]. Cause of anaemia was found in 10 out of 27 (37.03%) patients in the IDA group. Of the 10, 3 (30%) cases were of malignancy while 2 (20%) each were of haemorrhoids and duodenal ulcer. There was one case (10%) each of rheumatoid arthritis, ITP and diabetic nephropathy. 17 of the 27 (62.96%) patients had IDA without any gastrointestinal blood loss. These could be due to nutritional factors. In ACD, we could find a possible cause in 28 of the 50 (56%) cases. Of these, 10 (35.71%) had either active or healed pulmonary tuberculosis. Those with treated tuberculosis often had secondary infection. 6 of 28 each i.e. 21.42% had chronic renal insufficiency, and significant chronic airway disease. Only 2 (7.14%) cases of malignancy were detected in this group. There was one case each of alcoholic liver disease (fatty liver), cirrhosis of liver, bronchiectasis, pelvic inflammatory disease and chronic cholecystitis. In the remaining 22 cases where there was no history of chronic disease and the investigative parameters were in favour of ACD. These were labeled as undetermined causes. No detailed investigations were done in these cases due to limitation of protocol. It is possible that more causes could have been determined if they were investigated in more detail. Macrocytic anaemias occurred without any detectable cause in most of the patients (8 of 9 i.e. 88.89%) in our study. The lone patient where cause

could be found was alcoholic. Cases where no cause was found could be nutritional. Further etiological classification of macrocytic anaemia was not done in our study.

The 4 causes in the other group include 2 leukaemias (microcytic and normocytic one each), one lymphoma (normocytic) and one of aplastic anaemia (macrocytic). Comparing with other similar studies, the common causes in the 15 hospitalized patients of anaemia in the study by **Matzner Y et al**[06] were: chronic renal failure (4), metastatic carcinoma, & gastrointestinal bleeding (3 each). In the population based study by **Campbell AJ et al**[07] in 19 patients of anaemia the common causes were malignancy & renal insufficiency (6 each). In the study by **Joosten E et al**[16] the common causes of anaemia in 178 hospitalized patients were: Chronic disease (35%), Iron deficiency (15%) and unexplained causes (17%). In the study by **Sahadevan et al**[17], of the 54 anaemic patients the commonest causes were folate & B_{12}deficiency (15), and undetermined causes (22).

SUMMARY AND CONCLUSIONS:

Present study was carried out in the Acharya Vinoba Bhave Rural Hospital from August 1, 2003 to January 15, 2005. A total of 90 elderly patients, 49 males and 41 females were evaluated for a possible cause of anaemia. The maximum numbers of patients (20 males and 15 females) were in the age group 60-64 years. Males and females were comparable in age and mean haemoglobin. There was no significant difference in the mean haemoglobin levels as age increases. Morphologically, most of the patients (53) had microcytic anaemias, while the next common was normocytic anaemias (27). In our study, microcytic anaemias were more common in females. Macrocytic anaemias were more severe in our study. All the IDA patients in our study were microcytic while in ACD a good number of them (50%) were microcytic. Mean MCV in IDA was significantly lower than that of ACD in microcytic anaemias (p=0.0003). Of the 90 patients, only 5 had stool for occult blood positive. Majority of patients with IDA did not have evidence of blood loss through gastrointestinal tract. Majority had no incriminating drug history. Marrow iron staining is a simple and effective way to differentiate between IDA and ACD amongst microcytic anaemias in majority of the cases. ACD (55.5%) is the most common type of anaemia seen in elderly patients in this study, next common being IDA (30%). In 46.6%of the cases possible cause of anaemia could be found. The remaining cases could be nutritional in origin, due to aging or due to undetermined causes. Cause of anaemia was found in 37% of the patients in the IDA group and in 56% of the patients in ACD group. Tuberculosis and chronic renal insufficiency were the common causes found in ACD. Marrow disorders and leukaemia/lymphoma were found to be the cause in only 4.4% of the cases. Causes of anaemia in ACD group were based on examination and relevant investigation findings only. No special effort was made to document any disease other than that warranted by clinical assessment. A population-based study will better reflect the prevalence and causes of anaemias in asymptomatic elderly subjects.

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