Original Article

Does aging have an impact on hemoglobin? Study in elderly population at rural teaching hospital

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Abstract

Background: The prevalence of anemia increases with age. Some serious underlying conditions may lead to anemia in the old age. The present study was undertaken to detect and do morphological typing of anemia and further delineate etiological factors in elderly patients. **Methods:** In this hospital-based prevalence study carried out a tertiary care center over one and half years, a total of 90 patients were fully evaluated for etiology and typing of anemia in elderly (>60 years age) patients. Details of other significant medical and surgical history were noted. Laboratory investigations were conducted, which included complete hemogram, peripheral blood smear, reticulocyte count, erythrocyte sedimentation rate estimation, serum urea, serum creatinine and serum lactate dehydrogenase, bone marrow examination (with Prussian blue marrow iron staining), serum iron and serum total iron-binding capacity, serum ferritin, and stool and urine examination. **Results:** The mean hemoglobin as per age was 60–64 years- 5.95 gm%, 65–69 years - 6.7 gm%, 70–74 years - 6.58 gm%, and 75–79 years - 6.87 gm%. The difference not being significant (p = 0.33). Morphologically, 53 patients (24 males and 29 females) had microcytic anemia, 27 (17 males and 10 females) had normocytic anemia, and 10 (8 males and 2 females) had macrocytic anemia. Anemia of chronic disease (ACD) was the most common occurrence (50, 55.56%), followed by iron deficiency anemia (IDA) (27, 30%), macrocytic anemia (9, 10%), and others 4 (4.44%). The cause of anemia was found in 10 out of 27 (37.03%) patients in the IDA group, 28 out of 50 (56%) in the ACD group, whereas the etiology was discernible in only one out of nine cases (11.1%) of macrocytic anemias. **Conclusion:** There was no significant difference observed in the mean hemoglobin levels as the age increased. Morphologically, the majority of the patients had microcytic anemia, followed by normocytic anemia. A population-based study is recommended for further assessment of the prevalence and causes of anemias in asymptomatic elderly subjects.

Keywords: Anemia, elderly, morphological types, rural hospital

Introduction

The world population is aging. India, particularly, is undergoing a demographic transition, with a shift to a higher proportion of elderly (increased from 5.6% in 1961 to 7.4% in 2001).[1] The symposia "Anemia in the Elderly: Clinical Impact and Practical Diagnosis" took place during World Congress of Gerontology, held at Vancouver, Canada on July 4, 2001.[2] One of the predominant themes that emerged from this symposium was that the prevalence of anemia increases with age. Using the World Health Organization criteria for anemia [Hemoglobin (Hb) less than 12 g/dl in non-pregnant women and less than 13 g/dl in men], the prevalence of anemia has been shown to be ranging from 6% to 30% in men and 10% to 22% in women.[3]

In most elderly patients, an underlying cause of anemia is found for Hb levels less than 12 g/dl.[4] However, there are speculations and suggestions that lower standard laboratory values for Hb and hematocrit be used for patients older than 65 years of age.[5] This,

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in part, is a result of a high prevalence of mild anemia and the relative frequency at which no obvious etiology can be identified.

Several factors, some serious, have been identified to cause anemia in this age group, e.g. blood loss or chronic disease.[4,5] In some cases, the cause may remain unknown as a result of the presence of comorbid conditions masking symptoms of anemia. Therefore, appropriate diagnosis and management strategies of anemia in the elderly seem imperative. The present study was undertaken with the objective of detection and morphological typing of anemia and further delineation of underlying etiological factors in elderly patients coming to a tertiary care rural health set-up, along with the planning of preventive and therapeutic guidelines for the same.

Methodology

This hospital-based prevalence study was carried out at a tertiary care rural health set-up over the period of one and a half years (August 2016 to January 2018). The study population consisted of all the elderly patients routinely attending to the hospital for various ailments. All the patients admitted to the Medicine wards in the hospital during the study period were considered for the study under the following selection criteria:

Inclusion criteria

- Patients aged more than 60 years (both males and females)
- Hemoglobin level of less than 10 g/dl.

Exclusion criteria

- Any obvious history of blood loss (e.g., bleeding piles)
- Established cause of anemia (e.g., diagnosed chronic renal failure (CRF)/malignancy)
- Any acute life-threatening illness
- Refusal to give consent.

Approval from the Institutional Ethics Committee was obtained before the commencement of the study. All the eligible patients were enrolled sequentially after written informed consent and identification details such as name, age, sex, place of residence, and indoor registration number were recorded. A detailed history of present illness was noted. Symptoms specific for particular anemia such as paresthesia, ataxia and diminished proprioception, and chronic infection were also enquired into. Details of other significant medical and surgical history were noted. History of alcohol consumption and usage of medications [e.g., Non-steroidal anti-inflammatory drugs (NSAIDs), antineoplastic agents, and phenytoin sodium] were also asked for. Detailed physical examination was conducted, which included general and systemic examination, along with per rectal/proctoscopic examination and gynecological examination (per-vaginal and per-speculum) in females. Laboratory investigations were conducted, which included complete hemogram, peripheral blood smear, reticulocyte count, erythrocyte sedimentation rate estimation, serum urea, serum creatinine and serum lactate dehydrogenase, bone marrow examination (with Prussian blue marrow iron staining), serum iron and serum total iron-binding capacity (TIBC), serum ferritin, and stool and urine examination, as indicated.

The morphological typing of anemia was according to mean corpuscular volume (MCV): macrocytic (>100 fl), normocytic (80–100 fl), and microcytic (<80 fl).[6] Iron deficiency anemia was diagnosed when the serum ferritin was decreased or when a decreased serum iron was accompanied by an increased TIBC, with the transferrin saturation being less than 10%. Anemia of chronic disease (ACD) was diagnosed when the serum ferritin was normal or elevated or when both the serum iron and TIBC were decreased, with the transferrin saturation in normal range. Macrocytic anemia was diagnosed by blood and bone marrow picture.[6]

Statistical analysis was performed using SPPS (version 12) and the GraphPad instant software. Chi-square, unpaired *t* test, ANOVA, and Fischer exact test were employed and the significance was considered at $P < 0.05$.

Results

Initially, a total of 110 patients were considered for the study, out of which 20 were excluded (12- obvious history of blood loss, 3- known case of malignancies, 3- acute life-threatening illnesses, and 2- drop outs). Hence, a final sample of 90 participants was studied further. Of these, 49 were males and 41 females, with maximum patients in the age group 60–64 years (35, 38.9%) followed by 65–69 years (32, 35.6%). There was insignificant difference in the mean age of male participants (65.67 ± 4.69 years) and female participants (64.53 ± 3.97 years).

The mean Hb in males was 6.44 ± 1.68 gm% and females was 6.28 ± 1.98 gm%, the values being comparable statistically (p = 0.68). The mean Hb in the mentioned age categories were observed as follows: 60–64 years - 5.95 gm%, 65–69 years - 6.7 gm%, 70–74 years - 6.58 gm%, and 75–79 years - 6.87 gm%. There was no significant difference in the mean Hb levels observed with the increasing age (p = 0.33). The age-wise distribution of Hb is as detailed in Table 1.

Morphologically, a total of 53 patients (24 males and 29 females) had microcytic anemia, 27 (17 males and 10 females) had normocytic anemia, and 10 (8 males and 2 females) had macrocytic anemia. 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 anemia observed among females. The females had significantly lower mean MCV (72.34 ± 16.58 fl) than the males (80.38 ± 18.2 fl) (p = 0.03). There was no significant decrease in the MCV observed with increasing age (p = 0.11). The mean MCV in microcytic anemia was 64.69 ± 7.57 fl, in normocytic anemia was 86.6 ± 4.52 fl, and that in macrocytic anemia was 113.79 ± 9.8 fl. The MCV in three types of anemias

was not significantly different ($P > 0.05$) in males and females shown in Table 2.

Of the 90 patients, only 5 had stool for occult blood positive. Of these, 4 had microcytic anemia and 1 had normocytic anemia. Of these, 2 had peptic ulcer on upper gastrointestinal endoscopy, whereas one had a growth in the rectal wall on proctoscopy. Seven patients (3 males and 4 females) had a positive incriminating drug history (NSAIDs in all cases). Of these, 3 had microcytic and 3 normocytic anemia and one had macrocytic anemia.

Serum iron was found normal in 19 (21.34%), low in 70 (78.65%), and one patient had high. Of the 70 patients with low serum iron, 48 (68%) had microcytic anemia, 19 (27%) normocytic anemia, and 3 (4%) had macrocytic anemia. Bone marrow iron staining was done in all 90 cases. Marrow iron was absent in 22 cases, whereas iron stores were present in 65 cases, with 3 slides being inconclusive. The mean MCV when bone marrow iron was absent was 63.41 ± 12.98 fl, whereas it was 80.75 ± 17.46 fl when the marrow iron was present. When the cut-off for decreased marrow iron was raised to <3+, the mean MCV was 71.12 ± 16.5 fl, versus the 77.01 ± 18.66 fl mean MCV observed when the marrow iron was ≥3+. This difference in MCVs was extremely significant statistically ($P < 0.001$). Out of 53 patients with microcytic anemia, 20 (37%) had absent marrow iron, 16 (30%) had <3+ and 16 (30%) had ≥3+ marrow iron.

Table 1: Distribution of hemoglobin values across different age categories

Age (Years)	60-64		65-69		70-74		75-79	
Hb (%)	Male	Female	Male	Female	Male	Female	Male	Female
2.1-4.0	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 2: Comparison of mean MCV in males and females across various anemia morphologies

Anemia morphology	Microcytic	Normocytic	Macrocytic
Overall	64.64±7.57	86.6±4.52	113.79±9.8
Males	65.7±7.25	85.84±3.91	112.81±7.83
Females	63.85±7.86	87.88±5.43	117.7±19.94
P	0.88	1.13	0.34

Table 3 details the age and gender-wise distribution of various types of anemias observed in the present study. ACD was the most common occurrence (50, 55.56%), followed by iron deficiency anemia (IDA) (27, 30%), macrocytic anemia (9, 10%), and others 4 (4.44%). The four others included 2 cases of leukemia's and one each of lymphoma and aplastic anemia. The mean Hb did not vary significantly between genders across, but it did vary significantly across various types of anemia (IDA- 6.24 ± 1.76, ACD- 6.76 ± 1.62, macrocytic anemia- 4.64 ± 1.98, and others- 6.2 ± 2.6) (p = 0.012).

All the patients with IDA (n = 27) had microcytic morphology, of those having ACD, 25 (50%) each had microcytic and normochromic picture. The mean MCV of those with IDA was 61.05 ± 7.58, with ACD was 77.59 ± 10.6, and those with macrocytic anemia was 112.73 ± 9.78, the intertype differences being highly significant ($P < 0.001$). All 27 patients of IDA had low transferrin saturation consistent with the diagnosis of IDA, whereas 24 of 27 patients (88.9%) had high TIBC and low serum ferritin. All the 27 had <3+ marrow iron and low serum iron. In ACD of microcytic type (n = 25), 24 (96%), patients had high to normal transferrin saturation and all of them had normal to low TIBC and normal to high serum ferritin. In ACD of normocytic type, all 25 had normal to high transferrin saturation and serum ferritin, whereas 24 (96%) had normal to low TIBC. Seven of them (28%) had normal serum iron, whereas 18 out of 25 (72%) had low serum iron. Among macrocytic anemia, all 9 patients had normal to high transferrin saturation and normal serum ferritin.

The cause of anemia was found in 10 out of 27 (37.03%) patients in the IDA group, 28 out of 50 (56%) in the ACD group, whereas the etiology was discernible in only one out of nine cases (11.1%) of macrocytic anemias.

Discussion

There was no significant difference observed in the mean Hb levels as the age increased. This is similar to the study by Matzner *et al.*, who observed the fall in Hb not getting sharper with age.[7] Malnutrition has been purported to be one of the confounders responsible for declining Hb levels found in old age rather than old age itself.[8] The mean Hb levels between genders was comparable. In contrast to our finding, Matzner *et al.* found that mean Hb level for men was significantly higher than women.[7]

Morphologically, the majority of the patients (53, 58.9%) had microcytic anemia, followed by normocytic anemia. While Salive

Table 3: Age and gender-wise distribution of types of anaemias

Age	60-64 years		65-69 years		70-74 years		75-79 years		Mean Hb (gm%)		*P*
Type	M	F	M	F	M	F	M	F	Male	Female	
IDA	4	7	3	9	2	2	0	0	6.62±1.2	6.06±2.03	0.46
ACD	8	7	8	10	11	2	2	2	6.94±1.34	6.52±1.92	0.37
Macrocytic	5	1	0	1	2	0	0	0	4.31±1.77	5.8±3.11	0.39
Others	3	0	1	0	0	0	0	0	6.2±2.6	0	-

et al. had observed majority of patients (80%) to have normocytic anemia, a finding confirmed later by Izaks *et al.* in a larger study.[9,10] This is partly explainable on the basis of relative lack in the intake of nutritional food, especially iron-rich food items, in the average Indian diet. The MCV levels expectedly went up from microcytic anemia, to normocytic anemia and macrocytic anemia. Females had significantly lower MCV than males, a finding consistent with that of Ania BJ *et al.* in a population-based study.[11] There was no significant decrease in the MCV with the advancing age, which is similar to the observations of Timiras *et al.*[12]

Of the 90 patients, only 5 had stool for occult blood positive. Seven patients (3 males and 4 females) had a positive incriminating drug history (NSAIDs in all cases). Of these, 3 had microcytic and 1 had normocytic anemia. Regular salicylate intake had been documented to be commoner in IDA, than in those not using salicylate excessively.[13] In addition, there remains a real possibility of under-reporting of drug usage.

The first stage of iron deficiency is a negative iron balance, during which iron stores start decreasing, evident by a decrease in serum ferritin level or decreased appearance of stainable iron on bone marrow examination. When iron stores start becomes depleted, serum iron begins to fall. Gradually, TIBC increases and transferrin saturation begins to fall, leading to impairing Hb synthesis. Microcytes make their first appearance in the peripheral blood smear, along with a decrease in the MCV. Gradually, Hb and hematocrit begin to fall.[13,14]

The fall in MCV was observed to be parallel to a decrease in marrow iron in the present study and the combined predictability of MCV and marrow iron staining together was 100%. Further, observations regarding marrow iron staining lead us to believe it as a simple and effective way to differentiate between IDA and ACD, especially when MCV and serum iron fail to distinguish. Patterson *et al.* reported serum iron to be performing poorly as a predictor of iron stores, which is not surprising as depressed serum iron levels occur in both IDA and ACD.[15] In ACD, all 50 patients uniformly had normal or above normal serum ferritin levels. It did not correlate consistently with the serum iron levels, which were low, and bone marrow stores, which were depleted in the majority of cases. The same goes with macrocytic anemia, where no consistent correlation was observed between marrow iron and serum iron levels.

Serum ferritin has been a most valuable addition to the assessment of iron stores and, in the uncomplicated iron deficiency; it is both highly specific and sensitive. Unfortunately, numerous conditions tend to elevate it in an older population. It appears to rise with aging but also with acute and chronic inflammatory conditions, particularly those affecting liver.[16] Serum ferritin level, along with TIBC and transferrin saturation, was found particularly valuable in ACD cases, where it was able to distinguish between ACD and IDA although the patient had microcytosis and variable iron staining and serum iron levels.

ACD (55.5%) was the most common type of anemia in elderly patients seen in the present study, followed by IDA (30%). This finding is consistent with most of the previous available [7,8,17,18] literature. Tuberculosis and chronic renal failure were the most common culprits in ACD bracket. However, more cases could have been detected with more extensive evaluation protocol, especially for the cases of ACD; which constitutes a limitation of the study. Again, macrocytic anemias could not be classified further because serum B_{12} and folate levels were not a part of the protocol owing to resource constraints.

Anemia, a disorder that appears quite simple at first look, can in fact be a marker of multiple significant underlying disorders. Thus, as proposed by O'Mahoney *et al.* and Powell DJ *et al.*,[19,20] a thorough workup by Primary Care physicians, who often act as the first point-of-contact for a majority of the population, can lead to higher specificity of diagnoses and thus better treatment results for patients. The increasing importance of this concept of in-depth primary care-based analysis of various etiological factors contributing to anemia in the elderly has also been brought to light in multiple other recent reports from international literature.[21-24]Keeping in mind the comparatively small sample size included in the study, the authors acknowledge that a larger population-based study will better reflect on the prevalence and causes of anemias in asymptomatic elderly subjects and is hence recommended.

Conclusion

There was no change in the mean hemoglobin levels as the age increases. In our study majority of the patients were having microcytic anaemia, followed by normocytic anaemia. However, larger population based study is recommended for further assessment of the prevalence and causes of anaemias in normal elderly subjects.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflict of interest

There is no conflict of interest.

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