

Original Research Article

Haematological Patterns of Anaemia in Geriatric Patients and its Etiology: A study of 500 cases.

ABSTRACT :

Introduction: Anaemia in the elderly is a global health problem, since it is associated with significant morbidity and mortality. WHO criteria consider anaemia when level of haemoglobin is less than 13g/dl in males and 12g/dl in females. Anaemia is easier to miss among the elderly because symptoms such as fatigue, generalized weakness, or mental confusion can be linked to the ageing process. However, anaemia should never be considered as a natural part of growing older.

Aim: To investigate the haematological pattern of anaemia and its underlying etiology in elderly Indian patients.

Materials and methods: A prospective study undertaken over a span of 2 years in a tertiary care hospital in Western Maharashtra. The study included 500 geriatric (>65years) anaemic patients who underwent a complete haemogram and the results were correlated with peripheral blood smear findings. Other diagnostic tests were done as indicated.

Results: The spectrum encompassed all patterns of anaemia with the most common being normocytic normochromic pattern (57.26 %). Overall, there was slight male preponderance (53%) with 65-74 years (69%) being the most common age group afflicted. Maximum number of elderly people had moderate anaemia (56%) in my this study; and Anaemia of chronic disease (27.2%) was the most common etiological cause of anaemia followed by iron deficiency anaemia (23.4%) in my study. Upper gastrointestinal lesions (59 %) were the most common causes of iron deficiency anaemia in the present study followed by nutritional deficiency (31.6 %).

Conclusion: Correlation of haemogram and peripheral blood smears is a crucial first step to advise subsequent investigations for assessing and diagnosing the etiology of anaemia. Thus, it plays a role in deciding the management protocol and contributes towards a better quality of life for geriatric anemic patients.

Key words: Anaemia of chronic disease; geriatric; haemogram; RBC indices; peripheral blood smear.

INTRODUCTION

Anaemia is defined as reduction in the concentration of haemoglobin in the peripheral blood which is below the normal levels for the same age and sex of the individual, and in the same environment. Anaemia is not a disease but an objective sign of disease and needs further evaluation to determine the underlying cause and appropriate treatment. ^[1]

Anaemia is the most common haematological disorder affecting humankind and is often observed in nutritional deficiencies and chronic disease states leading to diagnostic difficulties. ^[1,2]

Because of its high prevalence and accompanying severe morbidity and mortality, anaemia is a global health concern in the elderly population. The reported prevalence of anaemia in the elderly is 2.9%–51%. ^[3,4]

According to the World Health Organization (WHO) criteria, the level of haemoglobin less than 13 g/dl in case of males and less than 12 g/dl in females are considered as anaemia. ^[5]

Comment [A1]: Use full name: The World Health Organization's

Comment [A2]: This conclusion is different from the discussion and the conclusion in the main text of this manuscript. Please check and revise accordingly.

Comment [A3]: Use full words

Though anaemia is an extremely common and significant problem in the elderly, it often remains under-diagnosed and is not reported to the patient because it is mostly perceived as a mere consequence of aging.^[6]

In geriatric age group complications due to anaemia are more severe compared to younger adults and directly proportional to quality of life.^[7]

Anaemia of chronic disease (ACD) is a common cause of anaemia in the elderly and in admitted patients.^[2] ACD and iron deficiency anaemia (IDA) are common causes of anaemia. It's not easy to delineate the prevalence rate of such kind of conditions because they are often confusing and ACD is generally a diagnosis of exclusion.^[2] ACD is seen in several diseases such as malignancies, chronic infectious and auto-immune diseases, thereby indicating the multiplicity in pathogenetic pathways leading to it.^[2,8]

Other causes of anaemia in elderly can be Vitamin B12 or Folate deficiency, Upper GI ulcers, chronic gastritis, alcoholism, cancers, various hematological disorders or unexplained causes.^[8,9]

The initial approach to management of patients with anaemia is through the red blood cell (-RBC) indices and its correlation with peripheral blood smear findings. These indices form the basis of the morphological classification of anaemias as: nNormocytic nNormochromic, mMicrocytic hHypochromic and mMacrocytic pattern.^[1,8]

Comment [A4]: Use full words

The purpose of this study was to analyze the characteristics of haematological patterns of anaemia in elderly people and to obtain the most accurate etiological profile. Failure to examine anaemia in the geriatric age group may result in the delay in the diagnosis of potentially curable diseases being delayed.^[9]

MATERIALS AND METHODS

A prospective observational study undertaken over a span of 2 years from September 2019 to September 2021 in a tertiary care hospital in Western Maharashtra. The study encompassed a sample population of 500 geriatric (>65 years) anaemic patients who underwent a complete haemogram and the results were correlated with peripheral blood smear findings. Other tests like serum iron, serum total iron binding capacity, serum ferritin, serum folic acid, serum vitamin B12 and bone marrow aspiration/biopsy were done performed as indicated.

Sample size was calculated ion was done using Winpepi version 11.38. Institute Ethics Committee Clearance was obtained before the start of the study. The data for the study were as collected from the records of blood reports in the Central Clinical Laboratory. The pPurpose of the study was explained to the patient and written informed consent was taken after assuring the responders about the confidentiality of the data. Data collection was performed done using predesigned and pretested proforma.

Inclusion Criteria

- Patients who weare 65 years or older with haemoglobin less than 13g/dl in case of males and less than 12g/dl in females were ill be included in this study.

Exclusion Criteria

- Patients less than 65 years of age with haemoglobin higher than 13g/dl in case of males and higher than 12g/dl in females will be excluded from this study.
- Patients who had received a blood transfusion during the last 12 weeks and patients on chemotherapy or radiotherapy are excluded.

Comment [A5]: No need to mention this because they were not in the samples who were included in the first place.

[There should be a description on the grading criteria of anaemia in this study – there are 3 grades in the Table 1]

RESULTS

The present study was carried out on 500 anaemic elderly patients in the age group of 65 years and above. Table 1 indicates that, maximum number of subjects (69%) were in the age group of 65-74 years and the mean age was found to be 71.37 years. Gender wise, slight male predominance (53%) was

observed in the present study as compared to females. ~~Min my study, more~~ more than half of cases (56%) had moderate anaemia followed by mild (25%) and severe (19%) anaemia- (Table1).

Table 1: Age group wise grading of Anaemias

Age group (years)	Anaemia grade (%)			Total
	Grade 1	Grade 2	Grade 3	
65-74	87 (25.2%)	192 (55.7%)	66 (19.1%)	345
75-84	31 (23.8%)	72 (55.4%)	27 (20.8%)	130
85-94	7 (28%)	16 (64%)	2 (8%)	25
Total	125	280	95	500

Study of RBC indices and peripheral blood smears revealed that the most prevalent morphological pattern of anemia was normocytic normochromic (57.26%) ~~in my study~~ as shown in table 2:- followed by microcytic hypochromic (35.64%) and macrocytic (7.1%) patterns.

Table 2: Peripheral blood smear patterns in the study group

PBS findings	Number	Percentage
Normocytic, Normochromic	286	57.26
Microcytic, Hypochromic	178	35.64
Macrocytic	36	7.1
Total	500	100

It was observed that anemia of chronic disease (27.2%) was the ~~most commonest~~ most common etiological cause of anaemia, followed by Iron deficiency anaemia (23.4%) (Table3).

Table 3: Etiological distribution of anaemia in the study group

Causes	Number	Percentage
Iron deficiency anaemia	117	23.4

Anaemia of chronic disease	136	27.2
Hematological disorders	93	18.6
Chronic kidney disease	65	13
Folate/Vitamin B12 deficiency	17	3.4
Multifactorial	19	3.8
Hypothyroidism	8	1.6
Unexplained	45	9
Total	500	100

It was also observed in my study that upper gastrointestinal lesions (59 %) were the most common finding in patients with causes of iron deficiency anaemia followed by nutritional deficiency (31.6 %) (Table4).

Table 4: Causes of iron deficiency anaemia in the study group

Causes	Number	Percentage
Upper GI lesions	69	59
Chronic Gastritis	37	31.6
Gastric ulcer	9	7.7
Duodenal ulcer	8	6.8
Esophagitis	10	8.5
Celiac disease	5	4.6
Lower GI lesions	4	3.4
Terminal ileal ulcer	2	1.7
Caecum ulcer	2	1.7

Comment [A6]: It may be not totally correct to say that they are the cause. There is no evidence here. In epidemiological term, it is described as "having association"

GI malignancy	7	6
Nutritional	37	31.6
Total	117	100

We also found that Solid organ malignancies (34.6%) and liver diseases (30.1%) were among the important causes of anaemia of chronic disease. Other causes like Tuberculosis, Rheumatoid Arthritis, Osteomyelitis, chronic obstructive pulmonary disease (COPD), urinary tract infection etc were also common significant in geriatric age group. Myelodysplastic syndrome (22.6%) was found to be the most common hematological disorder causing anaemia in elderly people. Other hematological disorders causing anaemia are shown in table 5.

Table 5: Causes of Anaemia due to Hematological disorders in the study group

Causes	Number	Percentage
Myelodysplastic syndrome	21	22.6
Multiple Myeloma	6	6.5
Non-Hodgkin's Lymphoma	14	15
Hodgkin's Lymphoma	4	4.3
Chronic Myeloid Leukemia	15	16.1
Chronic Lymphocytic Leukemia	10	10.8
Aplastic Anaemia	3	3.2
Pancytopenia	20	21.5
Total	93	100

DISCUSSION:

Anaemia is a serious universal concern in the geriatric age group (65 years and older), and it is linked to poor clinical outcomes. Despite the fact that it is a major issue that must be treated on a priority basis, particularly in developing nations like India, it is frequently overlooked or ignored due to the more severe and attention-demanding ailments that affect the aged.

Since anaemia is recognized as a significant contributor to morbidity, mortality and frailty in the elderly patients, a better understanding of the patho-physiology of anaemia in this age group is necessary to provide a critical end point for intervention that will not only improve their survival but also raise the standard of their well being.

In the present study, total of 500 anaemic elderly patients in the age group of 65 years and above were studied. The main objective of our study was to identify the haematological pattern of anaemia and classify it on the basis of **h**Haemogram, RBC **i**ndices and correlate with **p**Peripheral **b**Blood **s**Smear. Also an effort was made to determine the closest possible etiological profile for these elderly patients.

-These patients were categorized into three groups (Table1) according to their age and it was observed that patients in the age group of 65-74 years (69%) were maximally affected by anaemia. This finding is in concurrence with Bhasin et al. study.^[9] The maximum age of the elderly anaemic patient in **my this** study was 93 years.

Males were found to be more anaemic (53 %) than females (47 %) in the present research of the geriatric age group. Guralnik et al., Beghe et al., and Bhasin et al. also found a similar gender-based distribution.^[9,10,11]

Female predominance was found in research by Jadhav M et al. and Singhal S et al.^[12,13] The gender disparity varies by location, and the fact that in a developing country like India, male patients have traditionally been more likely to seek medical attention than female patients may contribute to the male predominance in this study. The minor male preponderance may possibly be due to the fact that WHO anaemia standards are greater for males (13 g/dl) than females (12 g/dl).

Anaemia is classified on the basis of level of haemoglobin in the peripheral blood i.e. mild anaemia with haemoglobin > 10 g/dl, moderate anaemia with haemoglobin in the range of 7-10 g/dl and severe anaemia in cases when haemoglobin is <7 g/dl. In the present study, majority of the cases (56%) were found to be moderately anaemic which was in accordance with Singhal S et al.^[13]

Comment [A7]: The criteria in this part can be rephrased and put into the Materials and Methods section

Mild anaemia was present in 25.2% cases and 19.1% were severely anaemic in our study. Few studies had maximum number of cases in mild anaemic group as seen in studies done by Petrosyan I et al., Cherian M et al., Melku M et al., Hafiz F et al.^[14,15,16,17]

The lowest haemoglobin observed in **my this** study was 4.1 g/dl and the highest was 12.2 g/dl in men and 11.3 g/dl in women. The mean haemoglobin in **my this** study was 8.4 g/dl (moderate anaemia) which tally with studies like Hafiz F et al. and Sharma et al. where the mean haemoglobin was 8.1 gm/dl and 8.8 gm/dl respectively.^[18,17]

In our study, all the patterns of anaemia were evident but normocytic normochromic anaemia was the most common morphological type of anaemia in both the sexes accounting for 57.26%. Similar findings were observed in studies done by Soni PN et al., Saurabh R Shrivastava et al., Singh R et al. in which normocytic anaemia was found to be 78.86%, 79.4%, 37.68% respectively.^[7,19,20]

Microcytic pattern was seen in 35.64% of the cases followed by macrocytic (7.1%) anaemia. Microcytic picture is predominantly seen in iron deficiency anaemias. The most accurate technique to identify iron deficiency anaemia is to measure serum ferritin levels. Iron deficiency is almost guaranteed to occur when serum ferritin is less than 15 ng/mL. If the serum ferritin level is greater than 100 ng/mL, iron deficiency is unlikely. Although ferritin values in the range of 15 to 100 ng/mL are somewhat predictive of iron deficiency anaemia, patients with these levels may have iron deficiency anaemia, anaemia of chronic disease, or both. A bone marrow examination may be required to directly measure iron stores in order to determine which type of anaemia is present. It can also be done in cases where the patient does not show response to iron therapy.^[21,22]

Anaemia with an MCV >100 fL is known as macrocytic anaemia. MCV levels rise slightly as people become older, but not enough to cause major macrocytosis. Out of 36 cases of macrocytic pattern of anaemia, 11 patients had **v**itamin B12 deficiency, 6 patients had folate deficiency, 4 patients had hypothyroidism, 5 patients had chronic liver disease and 10 patients had **MDS** in the present study.

Comment [A8]: Use full words

The substantial percentage of Vit B12 deficiency anaemias indicate that, it should be looked for in each case of anaemia. Early diagnosis and supplements are often suggested because it is easily treatable.^[23] The prevalence of anaemia due to Folate deficiency was considerably lesser in the present study than that reported in the study of Riva et al.^[24]

In the present study, anaemia of chronic diseases is the commonest underlying cause of anaemia, followed by anaemia due to iron deficiency (Table 6). This finding is in concurrence with the study by Bhasin et al. and Guyatt et al.^[9,25] Other causes of anaemia include anaemia due to haematological disorders (18.6%), chronic kidney disease (13%), multifactorial (3.8%), Vitamin B12/Folate deficiency (3.4%), and hypothyroidism (1.6%). No etiology could be identified in 45 patients (9%). This tally with study done by Sharma et al.^[18]

Table 6: Comparative study of contributory causes resulting in anaemia

	Present study	Guyatt et al.	Bhasin et al.
Iron deficiency	23.4%	36.2%	30%
Chronic disorder	58.8%	43.6%	48%
Others	17.8%	20%	22%

Anaemia of chronic disease can be difficult to diagnose in the laboratory because both serum iron and transferrin saturation levels are often low. Furthermore, the term's clinical application has been inconsistent, with no clear explanation in most cases. Certain laboratory parameters, such as normal or increased iron stores, can, however, be used to help in diagnosis.

One major factor that is often overlooked that may contribute to the production of anaemia in the older population is the nutritional status, which is rarely seen in the affluent communities. In the low socio-economic group where other dietary deficiencies exist, anaemia is of much more frequent occurrence. The principal reason for inadequate nutritional status in the elderly is poor dentition. Majority of the subjects in our study were of low socio-economic class and had poor dentition.^[26]

In present study, 65 patients (13%) of anaemia suffered from chronic kidney disease. This analysis alone is significant enough to attract our attention towards the fact that Hb concentration and kidney function are associated. Anaemia develops early in the course of renal illness and worsens as renal function declines.

Kidney function usually declines with age. It has been demonstrated that, anaemia is more prevalent when creatinine clearance and serum erythropoietin are low. A creatinine clearance below 60 ml/min is a risk factor for anaemia.^[23]

When a CKD-patient with chronic kidney disease (CKD) also has diabetes, anaemia is more likely. Despite the fact that individuals with diabetes are constantly checked for a range of problems such as diabetic nephropathy, diabetic neuropathy and diabetic retinopathy, haemoglobin levels are usually overlooked. Haemoglobin reductions are common before the onset of overt diabetic nephropathy. This drop in haemoglobin might happen for a number of reasons. The kidneys produce about 90% of the hormone erythropoietin (EPO), which is responsible for red blood cell production. Hypoxia in the kidney results in an increase in the synthesis of erythropoietin, which increases erythropoiesis under normal physiological conditions.^[27]

As a result of the enhanced oxygenation caused by the synthesis of new erythrocytes, the kidney reduces erythropoietin production. On the other hand, Tubule-interstitial damage caused by diabetes, begins early in the course of the disease, even before a decrease in **GFR** or albuminuria is noticed. The body is unable to produce appropriate amounts of erythropoietin in response to hypoxic injury in the kidney as functional renal tissue diminishes in people with CKD. ^[27,28]

Comment [A9]: Use full words

Another frequent issue in diabetic individuals is the intake of drugs that may impair production of haemoglobin thus causing drug induced anaemia. Metformin, angiotensin-converting enzyme inhibitors, fibrates and thiazolidinediones are some of them. Finally, inflammatory mediators such as interleukins and tissue necrosis factor are produced as a result of systemic inflammation linked with microvascular illness in diabetic individuals. These mediators reduce the effect of erythropoietin on the production of erythroid precursors in the bone marrow. ^[28]

Other factors, while not unique to diabetic individuals, worsen anaemia in patients with CKD. Platelet dysfunction, which increases the risk of gastrointestinal bleeding, decreased erythrocyte survival duration (up to 30–60% of the usual 120 days), and haemolysis due to uremic toxin deposition are among them. The chronic blood loss from repeated phlebotomy for the purpose of laboratory studies and blood loss in the dialysis tubing and dialyzer after every haemodialysis management may further add to falling levels of haemoglobin in dialysis patients, particularly those on haemodialysis. ^[27]

Because of the potentially serious effects of anaemia in CKD, it is critical to recognise and treat anaemia as soon as possible. As a result, it is critical to monitor Hb and diagnose anaemia in diabetic patients. ^[27]

NSAIDs and anti-platelet factors are well known risk factors for anaemia. ^[26] Metformin has been linked to Vit B12 deficiency in recent years, most likely due to malabsorption caused by metformin in the ileum. So it is advisable to monitor **vitamin B12** levels in patients on metformin therapy.

In the present study, there were several cases with concomitant pathology of iron and **Vit-vitamin B12** deficiency anaemias. This emphasizes the importance of looking for additional causes of nutritional anaemias, even if one type of deficiency has been identified. ^[23] This becomes more important in our country owing to the fact that nutritional anaemias are easy, safe and less expensive to treat so we should not miss them out.

In many cases, no definite etiology could be established. These cases come under **unexplained** anaemia (UA). A detailed history taking, better general and systemic examination, laboratory investigations, including bone marrow studies would be helpful in finding a more specific cause of anaemia in these cases. According to several reports, unexplained anaemia is widespread and may be caused by Myelodysplastic syndrome in some patients. ^[6]

As a result of our research, the majority of anaemic old aged people have an underlying, curable explanation for their anaemia. It is also critical that the treating physician is aware of the coexistence of anaemia in the geriatric age group, even if the presenting symptom is due to something else. As a result, it's even more important to check for anaemia's grade and morphological type, as well as relevant etiologies associated with it and treatment options. Because normocytic normochromic anaemia is the most frequent finding on peripheral blood smear, it's crucial to note that a normocytic pattern in an anaemic elderly person shouldn't be overlooked.

Diet and nutrition of the elderly population should also be given due consideration. Regardless of the screening costs, it is recommended to carefully analyze each anaemic patient, given that the diagnostic tests used are realistic and justified. Given the link between anaemia and a lower quality of life, a full geriatric assessment should incorporate a thorough clinical and laboratory workup for the presence of anaemia and predisposing factors to determine the etiology.

CONCLUSION

Despite recent advances in diagnostic techniques, anaemia in the geriatric age group continues to be underestimated and inadequately reported, particularly when mild, necessitating investigation of even mild anaemia in this susceptible population. Failure to diagnose anaemia in geriatric age group could lead to delayed diagnosis of potentially treatable conditions. Longitudinal studies would be beneficial in

determining the mechanism of anaemia and, more crucially, in examining the potential impact of treatment therapies in the community-dwelling older population.

Non-specific symptoms like generalized weakness, fatigue, dyspnea on exertion, palpitation, anorexia, lack of concentration, drowsiness, lethargy, mental confusion etc should not be overlooked in the elderly people as they may indicate presence of anaemia.

Elicitation of complete socio-economic information becomes mandatory in order to identify the other associated risk factors in the geriatric population. An effort to reach etiological diagnosis should always be made by the treating physician before instituting any specific therapy. Better definitions of anaemia, as well as more comprehensive investigations such as bone marrow examination, aid in the identification of anaemia subtypes, allowing for faster and more precise diagnosis and treatment.

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