# ANAEMIA IN ELDERLY: A BENIGN CONDITION OR AN EARLY WARNING? - A HOSPITAL BASED STUDY

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## ABSTRACT

*Objective:* To determine the frequency of etiological subtypes of anaemia in geriatric patients in hospital practice.

*Study Design:* Descriptive study.

*Place and Duration of Study:* Department of Medicine, PAF Hospital Islamabad, from September 2012 to August 2013.

*Patients and Methods:* One hundred elderly patients, aged ≥ 65 years and fulfilling the WHO criteria of anaemia were selected by non probability convenient sampling. Patients were classified according to the severity of anaemia as well as type of anaemia based on morphological findings. Based on clinical evaluation and further laboratory investigations etiological subtypes of anaemia were identified.

*Results:* A cause was determined in 91% patients. Anemia was multifactorial in 19% cases. Iron deficiency anaemia was detected in 42% with 27% subjects having iron deficiency as the sole cause. B12 and folate deficiency was detected in 10% and 7% patients respectively. Anaemia of chronic disease was present in 53% of the patients with renal insufficiency as the most frequent pathology seen in 11% patients. Underlying malignancy was diagnosed in 5% of the total study population.

*Conclusion:* Anaemia in elderly is often multifactorial. A basic workup can reveal the cause of anaemia in most patients. Iron deficiency anaemia is a readily correctible cause of anaemia that frequently results from blood loss in geriatric patients. Occult disease in particular malignancy must be ruled out in all anaemic elderly individuals. Early diagnosis and management of anaemia can have a significant impact on the overall disease outcome in elderly patients and should be part of a comprehensive geriatric assessment.

**Keywords:** Anaemia; Anaemia of chronic disease; Elderly; Geriatric; Iron deficiency anaemia; Multifactorial anaemia.

## INTRODUCTION

Geriatric health is a neglected area in developing countries like Pakistan. Hence it becomes increasingly important to recognize and address common medical problems which can have a significant impact on the quality of life in the elderly. Anaemia is one such problem the potential significance of which is generally not recognized. It has rightly been called "an emerging problem for the 21st century"[1]. Prevalence ranges from 10% in the community to 40% in hospitalized patients as reported in literature[2]. The clinical approach to evaluation of anaemia in elderly is evolving. What was considered to be in the past a mere consequence of aging is now considered to be not only a possible marker of underlying disease but also an independent risk factor for declining quality of life, cognitive impairment and morbidity with increased risk of hospitalization[3]. Den Elzen and colleagues while analyzing data from Leiden -85-plus Study have concluded that anaemia is an independent predictor of mortality[4]. There is now sufficient evidence to suggest that even mild anaemia in elderly can result in several adverse functional outcomes. The evaluation of anaemia in elderly can be challenging as multiple

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etiologies are often involved. Many patients have superimposed nutritional deficiency in a setting of a prior co morbid like renal disease or arthritis. No separate evidence-based guidelines currently exist with little consensus on definitions of different types of anaemia in this age group. Furthermore, most of the data is based on results from community dwelling adults in population based studies and cannot be applied to hospitalized patients.

**Aim**

The aim of this study was to evaluate anaemia in our elderly patients in hospital practice by means of a basic workup that can be utilized by most of our clinicians and to highlight the therapeutic and prognostic implications of an early diagnosis of anaemia in these patients. To our knowledge no such study has been conducted in Pakistan so far.

## PATIENTS AND METHODS

This descriptive study was conducted in the Department of Medicine, Pakistan Air Force Hospital Islamabad form September 2012 to August 2013 in collaboration with the Department of Pathology. The study was initiated after the approval of study proposal by the Hospital Ethics Committee after incorporating its suggestions to protect the patient's confidentiality. All the elderly patients (65 years and above) reporting over a 12 month period, either outdoor or indoor and fulfilling the World Health Organization (WHO) criteria of anemia[5] (hemoglobin <13 gm/dL in males and <12 gm/dL in females) were included. Patients were selected by non probability convenient sampling after informed consent. The age of 65 years was used as a cutoff point as it is widely accepted and most utilized in previous studies. Patients with a history of malignancy, recent surgery, blood transfusion or those already under treatment for anaemia were excluded. The patients were classified according to the severity of anaemia as well as morphological type of anaemia based on red blood cell indices and examination of peripheral film. Three grades of

anaemia were differentiated as per WHO criteria viz. Mild (haemoglobin between 11g/dl and lower limit of normal), moderate (haemoglobin between 8 g/dl and 10.9 g/dl), and severe (haemoglobin <8g/dl)[5]. Patients were analyzed on the basis of their symptoms, clinical findings, dietary habits and medication usage.

Complete blood counts with examination of peripheral smear, serum ferritin, vitamin B12 and folate assays were performed in all patients under study. We used the same reference ranges for the various tests as established by our laboratory. Complete blood counts were generated through Sysmex KX-21 haematology analyser with routine quality control. Peripheral blood films were examined after staining with Leishmann stain and a brilliant cresyl blue stained preparation was also examined in all cases for reticulocyte percentage. Renal function tests (urea, creatinine, sodium and potassium), liver function tests (bilirubin, alanine transaminase, alkaline phosphatase), lipid profile (total cholesterol, low density lipoproteins, high density lipoproteins and triglycerides), electrocardiogram (ECG), erythrocyte sedimentation rate (ESR) and C- reactive protein (CRP) were additionally performed to look for any underlying disorders if clinically indicated. An attempt was made to perform endoscopic evaluation in all patients suspected of gastrointestinal (GI) blood loss. Bone marrow examination was carried out in patients with abnormal cell counts or peripheral smear. Further relevant investigations, such as imaging studies, sputum for AFB, auto immune profile, rheumatoid arthritis serology and hepatitis serology were done as deemed necessary to reach a final diagnosis. Patients were classified into following etiological subtypes[6-8].

**Anaemia secondary to micronutrient deficiency**

Defined as one with deficiency of at least one of the three major micronutrients viz. iron, vitamin B12 or folate. Following subtypes were identified; Iron deficiency anaemia (IDA): A serum ferritin level <12 ng/dl or normal ferritin

but absence of demonstrable iron in the bone marrow with Perl stain. Anaemia secondary to cobalamin/B12deficiency: serum B12 <170 pg/ml; Anaemia due to folate deficiency: serum folate <3 ng/ml.

**Anaemia of chronic disease (ACD)**

Patients with anaemia secondary to chronic infectious, inflammatory, autoimmune or malignant disorder. Along with these, patients had either stainable iron in the bone marrow macrophages with reduced/absent siderocytes and sideroblasts and a raised ESR or CRP. Serum ferritin was normal or raised.

**Unexplained anaemia (UA)**

Patients in whom no cause could be

difference in frequencies of IDA in males and females. *p*-value of less than 0.05 was considered significant at 95% confidence interval.

## RESULTS

A total of 100 patients were studied during 12 month period. There were 47 male and 53 female patients. Age ranged from 65-90 years (mean age 73.16 years ± 6.1 years). Frequencies of mild, moderate and severe anemia in our study were 57%, 30% and 13% respectively. Normocytic normochromic anaemia was the dominant morphological pattern seen in 49% patients. Microcytic hypochromic anaemia was found in 37% while 14% had macrocytic anaemia. More than one etiology of anaemia was present in 19/100 (19%) patients.  Table-1 shows the main

**Table-1: Causes of anaemia in elderly patients.**

| Type of anaemia | No of patients | Percentage |
|---|---|---|
| Anaemia of chronic disease only | 39 | 39% |
| Iron deficiency as the only cause | 27 | 27% |
| B12 deficiency as the only cause | 5 | 5% |
| Folate deficiency as the only cause | 1 | 1% |
| Multifactorial anaemia including mixed deficiency anaemia | 19 | 19% |
| Unexplained anaemia | 9 | 9% |
| Total | 100 | 100% |

**Table-2: Causes of blood loss in the iron deficiency anaemia group (n=13).**

| Cause of blood loss | No of patients |
|---|---|
| Gastritis | 3 |
| Peptic Ulcer | 2 |
| Varices | 2 |
| Hemorrhoids | 2 |
| Ulcerative colitis | 1 |
| Malignant colonic polyp | 1 |
| Bleeding per vagina | 1 |
| Hematuria | 1 |
| Total | 13 |

identified were said to have UA. It was basically a diagnosis of exclusion.

Data was analyzed using IBM SPSS 20. Categorical data was calculated as frequencies and percentages. Mean and standard deviation were calculated for age. The chi-square test was used to look for any statistical significant

causes of anaemia in our elderly patients.

Owing to coexistence of multiple etiologies in a significant number of patients, the overall frequency of each etiological subtype of anaemia in the study population was determined as follows:

**Anaemia secondary to micronutrient deficiency**

Anaemia due to micronutrient deficiency was seen in 53/100 (53%) patients. Vitamin B12 and folate deficiency was found in 10/100 (10%) and 7/100 (7%) respectively. Majority of the patients (42/100 or 42%) patients had evidence of iron deficiency which included 27 (27%) with iron deficiency as the only cause while the rest of the 15 patients had other concomitant causes of anaemia along with iron deficiency. More than half of the female patients in our study (28/53 or 52.8%) were found to be iron deficient as compared to 15/47 (31.9%) of their male counterparts. The association between IDA and female gender was statistically significant (*p* value = 0.034).

On further evaluation, 13/42 (30.95%) patients with IDA were found to have blood loss anaemia. Table-2 depicts causes of blood loss anaemia in the iron deficiency group.

**Anaemia of chronic disease (ACD)**

ACD was diagnosed in 53/100 (53%) patients. Fig shows various pathologies underlying ACD in this study.

**Unexplained anaemia**

In 9/100 (9%) patients no cause of anaemia was identified even after investigations.

## DISCUSSION

The frequency of moderate to severe anaemia in our study was higher than most population based studies[9]. This is explained by the fact that it was a hospital based study conducted on geriatric patients with significant health problems health problems rather than on ambulant patients. In terms of morphological pattern, normocytic normochromic anaemia was less prevalent than expected and in contrast to the Western studies[10], a relatively higher percentage of the patients in our study (37% vs. 16.9%) were found to have microcytic anaemia. A logical explanation of this is the fact that an overwhelming majority of Pakistani population suffers from IDA which is a common cause of microcytic anaemia[8]. A significant number of patients in our study were found to be iron deficient (42%). Studies from the West by Price et al and Artz et al show much lower figures for IDA i.e 12% and 25.3% respectively[11,12]. In a recent Indian study Bhasin and co-workers have reported the frequency of IDA as 30% which, like our study, showed higher prevalence of IDA in the females reflecting similar demographic and socioeconomic background of these two countries[13]

IDA in this age group is often associated with gastrointestinal bleeding and malignancy and warrants further investigation before commencing iron replacement therapy. Most Western studies suggest IDA to be a consequence of blood loss rather than malnutrition[14]. While a significant 30.9% patients in our IDA group (reflecting 13% of the total study population) had evidence of blood loss anaemia, nutritional component remained predominant in this study. Hence the findings of our study are in accordance with the National Health and Nutrition Examination Survey (NHANES) 111, which classifies IDA with other nutritional anaemias, a classification more applicable to the third world countries[7]. The frequency of B12 and folate deficiency in our study was 10% and 7% respectively, reflecting the high prevalence of these deficiencies in Pakistani population as suggested by several local studies[15].

The prevalence of chronic diseases such as renal insufficiency, diabetes, atherosclerosis, arthritis, myelodysplasia etc rises dramatically with increasing age. Much work has been done in recent years to unfold the association of anaemia with many such diseases[16,17]. Main factor in the pathogenesis of ACD is increased level of hepcidin. Other contributing mechanisms result from increased levels of inflammatory cytokines such as interleukin (IL)-1, IL-6, tumour necrosis factor (TNF) and transforming growth factor (TGF)-$\beta$ to reduce the sensitivity of erythroid progenitors to erythropoietin. The previously used terminology of 'anaemia of chronic disease' is therefore now used interchangeably with the more appropriate term of 'anemia of

inflammation', also incorporating conditions like trauma, fracture and infections common in this age group[7]. Thus depending on the setting and diagnostic criteria used, the prevalence of ACD in elderly ranges from 26%-62.1% worldwide [8,9].

In our study, 53% of patients were found to have ACD with renal disease as the most frequent underlying pathology seen in 11%. Although glomerular filtration rate (GFR) is a more accurate tool, we used serum creatinine for the diagnosis of renal insufficiency in our study as it was more practical and is otherwise reliable at a cut-off value (>1.2 mg/dl for females and >1.5mg/dl for males). Our results are therefore comparable with a recent German study utilizing similar diagnostic criteria and reporting the frequency of renal insufficiency as 19.4%[18].

One of the most significant aspects of our study is that it highlights the association of anaemia with occult malignancy. In an unfortunate 5% of patients in this study, anaemia workup eventually led to the diagnosis of a previously unknown underlying malignancy. While this frequency is in accordance with most studies worldwide[19], considering the small sample size of our study, these numbers are quite

IDA or UA must be screened for underlying malignancy. In fact, early myelodysplasia is strongly implicated as one of the possible causes of UA in elderly [11,12,20].

UA has been shown to contribute up to a third of all anaemias in epidemiological surveys[11]. However, the frequency of UA was 9% in our study which is significantly lower. This discrepancy can be explained by the fact that in hospital settings, patients frequently report with an ongoing illness and also undergo a more extensive workup. In a recent hospital based European study frequency of UA was found to be 8.4%[21] while an Indian study with similar setting reports the frequency of UA as even lower i.e. 2%[13].

Strikingly, and as also recorded earlier[20,21] a considerable number of our patients were found to have multi-factorial anaemia and majority of these patients had superimposed IDA in the background of ACD. There is now conclusive evidence to suggest that correction of iron deficiency can significantly impact the outcome in chronic conditions like congestive heart failure, renal disease and arthritis[22,23]. Despite that, screening and treatment of IDA in geriatric
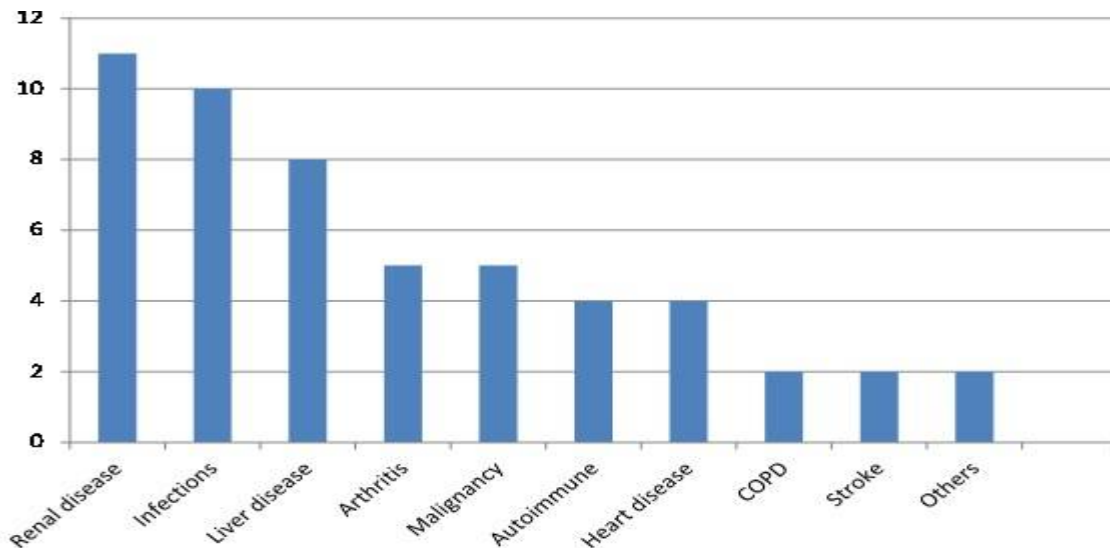


**Figure: Frequency of patients with anaemia of inflammation.**

alarming. Anaemia has been recognized as one of the leading indicators of cancer. Consequently, all anaemic elderly patients in particular those with

patients is often neglected.

Our study has certain limitations. We have used the WHO criteria of definition of anaemia

because it is widely recognized, but some studies propose age- adjusted criteria for the diagnosis of anaemia in elderly[24]. Serum ferritin is a reliable first- line tool to diagnose IDA[25]. However in a setting of illness or comorbids it is sometimes difficult to differentiate IDA from ACD as many of the iron assays including ferritin are affected by acute phase responses. Extensive laboratory investigations including bone marrow biopsy can reveal the true diagnosis including occult hematological malignancy in many patients especially where cause of anaemia remains obscured. This was a major limitation and beyond the scope of our study. Despite these limitations, an underlying cause of anaemia was diagnosed in majority of our patients and in only 9% patients, anaemia remained unexplained.

## CONCLUSION

The results of our study suggest that a basic workup can reveal the cause of anaemia in most elderly patients. Iron deficiency anaemia is a readily correctible cause of anaemia that frequently results from blood loss in geriatric patients. Occult disease in particular malignancy must be ruled out in all anaemic elderly individuals. Early diagnosis and management of anaemia can have a significant impact on the overall disease outcome in elderly patients and should be part of a comprehensive geriatric assessment. Critical next steps that must be taken include recognizing the multifactorial etiology and understanding better the mechanisms and possible treatment of UA in this vulnerable age group.

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## CONFLICT OF INTEREST

The authors have no conflict of interest to declare.

## AUTHORS CONTRIBUTION

Shamaila Burney was the primary writer of this article. Shamaila Burney and Saqib Qayyum Ahmed designed the study, contributed to data collection and extraction, providing clinical input and interpreting results. Rehan Masroor developed the statistical methods and performed the analysis.

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