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RESEARCH ARTICLE

STUDY OF MORPHOLOGICAL AND ETIOLOGICAL SPECTRUM OF ANEMIA IN ELDERLY IN A TERTIARY CARE CENTRE OF NORTH INDIA

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ABSTRACT

Anemia in the elderly patients is an extremely common problem that can be associated with mortality and impair the quality of life. Since anemia is a sign and not a diagnosis, therefore an evaluation is almost always warranted to identify its cause. (Bhasin and Rao, 2011) In our prospective study we investigated about the morphological type and the etiological spectrum of anemia in 100 patients with age 60 years and above. Hb< 12gm/dl (in females) and Hb<13gm/dl (in males) {acc to WHO Criteria} (World Health Organization, 2010) were the cut off value for anemia. The study population consisted of 66 male patients and 34 female patients with generalized weakness and easy fatigability as the most common symptom which was present in 100% of cases. The most common cause of anemia in elderly patients is anemia due to chronic kidney disease (35%) followed by iron deficiency (20%) than malignancy (15%), vitamin B12 and folic acid deficiency (14%), anemia of chronic inflammation (11%) and in 5% others including unexplained anemia. Overall the hematological causes were 50% and non-hematological causes were 46%. Normocytic normochromic (53%) anemia was the most common morphological type; was followed by microcytic hypochromic 30%) and then macrocytic as least common (17%). In geriatric age group hematological and non hematological causes were almost equal in our study that is comparable to other Indian studies and some western studies but the pattern vary from study to study indicates geographical variation in spectrum of etiology of anemia in elderly.

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INTRODUCTION

Anemia is a common concern in geriatric age group (more than 60 years of age) that is associated with mortality and poorer health-related quality of life, regardless of the underlined cause of the low hemoglobin. (Saurabh R Shrivastava *et al*., 2013) In elderly population, it can have significantly more severe complications than in the younger adults and can greatly affect their quality of life. (Ania Lafuente *et al*., 2001) Anemia can impair not only the quality of life but also there cognitive and physical functions of life and is a co-morbid condition that affect and even precipitates various diseases (e.g. heart disease, cerebrovascular insufficiency) and is even associated with increased risk of death. So, anemia should not be accepted as a consequence of aging and its cause must be explored. Studies indicate that the prevalence of anemia increases with advancing age and under age 75 years, anemia is more common in females, but over age 75 years it is more common in males. (Ferrucci *et al*., 2010) Some Indian studies by Bhasin *et al*. (2011), Shrivastava *et al*. (2013) and Prakash *et al*. (2015) showed slight difference in the spectrum of anemia in elderly. We conducted this study to evaluate the etiological spectrum and other characteristics of anemia in elderly patients in this north zone of India so that a known pattern can help to early diagnosis and management of patients.

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MATERIALS AND METHODS

It was a observational study which was conducted to study the morphological type and the etiological spectrum of anemia in elderly patients over a period of one year during 2014-15 at Pt. B.D. Sharma PGIMS Rohtak on 100 patients of age 60 years and above (either sex) presenting to our hospital fulfilling the WHO criteria of anemia Hb<13 in males and Hb<12 in females, coming to OPD or admitted in medicine ward. The patient selection was random and non-consecutive. After obtaining an informed consent, each patient's particulars with a detailed history was taken like history of nutritional status of

the patient, history of any drug intake especially NSAID's, drug history of any previous blood transfusion, history of any medical history e.g recent hospitalization, recent surgery, ESRD, previous chemotherapy or radiotherapy was enquired, history of alcohol abuse, history of bleeding (now or in past). Then detailed General physical and systemic Examination of the patient were carried out especially to see pallor, icterus, hepatomegaly, splenomegaly, lymphadenopathy, tachycardia, cardiac murmers, petechial spots etc. Following Routine hematological investigations was carried out in each and every case of anemia: hemoglobin (Hb), total leucocyte count (TLC), differential leucocyte count (DLC), absolute platelet count (APC), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), reticulocyte count, erythrocyte sedimentation rate (ESR), blood urea, serum creatinine, PBF – Peripheral blood film. Following Special Investigations was carried out in specific cases if required- Bone marrow eaxmination, Serum Vit B12 and Folic acid levels, Serum ferritin and transferrin level, UGI Endoscopy, Chest X- RAY, USG of abdomen and pelvis, stool for occult blood, proctoscopic examination, osmotic fragility test, coomb's test (both direct and indirect) etc. In our study we include patients with decreased kidney functions i.e. serum creatinine>1.5 mg/dl, gfr<60 ml/min/1.73 m^2 for more than 3 months duration with kidney damage detected by presence of imaging abnormalities radiologically like on ultrasound or pathological like on kidney biopsy. Data analysis was done with use of SPSS, version 13. Descriptive statistics was used to calculate the frequency, mean and standard deviation.

RESULTS

In our study population of 100 patients of age 60 years and above, 66 were males and 34 were females. The mean age of the patients was 66.07 years with S.D. of 5.95 years. Majority of patients (61) belonged to 60 - 65 years age group. Mean hemoglobin in 100 patients was (7.88 ±2.17) g/dl. Anemia was mild (9.5 – 12.9) g/dl in males and 9.5- 11.9 in females) in 25% of cases, moderate (between 8.0 - 9.5 g/dl) in 30% of cases and severe (below 8.0 g/dl) in 45% of cases. The mean value of MCV, MCH and MCHC were (87.47±14.15) fl, (28.76±5.52) pg/cell and (32.95±1.91)g/dl respectively in 100 patients. The most common symptom was generalized weakness and easy fatiguability in 100% of cases followed by shortness of breath (40%), decrease urine output (32%), pedal edema (18%), fever (15%), decrease appetite (14%), bleeding manifestations were observed in 8% of cases and loss of weight (5%) cases. Other symptoms like bodyache, abdominal discomfort were present in 3% of cases. Pallor was found in 100% of patients. Splenomegaly was present in 11% of patients and hepatomegaly in 6% of patients. Lymphadenopathy was present in 3 patients and 1 patient had icterus.

The characterization of anemia on peripheral smear in Fig. 1-.

Etiology of Microcytic hypochromic anemia

Microcytic hypochromic picture was observed in 30 patients out of total 100 cases. Complete iron profile were done in all suspected patients of microcytic anemia. Iron deficiency anemia was observed in 20 cases.

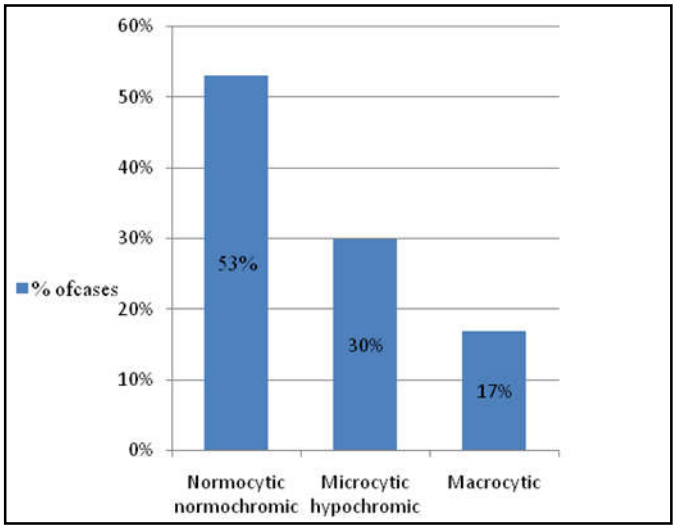

Fig. 1. Morphological type of anemia in elderly

Malignancy was observed in 5 cases. Anemia due to chronic renal disease was observed in 3 cases. Anemia of chronic inflammation was observed in 1 case and diagnosis remained unexplained in 1 case. Out of 20 patients of iron deficiency anemia, 9 patients had iron deficiency anemia due to chronic blood loss, 2 patients had GIT malignancy, 2 patients had nutritional deficiency whereas cause of iron deficiency anemia could not be determined in remaining 7 patients. Serum ferritin was low in all the 20 patients. Levels < 20 ng/ml was observed in 14 patients indicating severe iron deficiency whereas levels were between 20-100ng/ml in remaining 6 patients. Iron studies were done in all 20 patients which demonstrated that serum iron levels were low (<60mcg/dl) in all the 20 patients, iron binding capacity was increased (>350 mcg/dl) and transferrin saturation (<15%) was low in all the 20 patients. In 7 patients, stool for occult blood was negative, upper gastrointestinal endoscopy and colonoscopy was also normal. These patients were labeled as iron deficiency anemia but underlying cause of it was not known. Upper gastrointestinal endoscopy was done in all the patients of iron deficiency anemia. On UGIE (upper gastrointestinal endoscopy) 2 patients had multiple erosions seen in body and antrum of stomach. One patient had esophagitis with healing duodenal ulcer. One patient had hiatus hernia with lower esophageal ulcer. Two patients were diagnosed as alcoholic liver disease with portal hypertension with chronic blood loss in form of multiple and recurrent episodes blood in vomiting and stools, there UGIE revealed grade II, variceal bleed. On UGIE, Two patients revealed a mass lesion in body of stomach which was later diagnosed as CA stomach on biopsy (GIT malignancy). In 2 patients UGIE could not be done whereas it was normal in rest 7 patients of iron deficiency anemia. Two patients were having severe haemorroids that lead to chronic blood loss which was apparent on colonoscopic examination.

Etiology of Macrocytic anemia

Macrocytic picture was observed in 17 out of 100 patients. Serum Vitamin B_{12} and folic acid levels were done in all

suspected patients of macrocytic anemia.Vitamin B_{12} deficiency and folic acid deficiency was observed in cases. Vitamin B_{12} deficiency was observed in 5 cases, folic acid deficiency was observed in 1 case and combined vitamin B_{12} deficiency and folic acid deficiency was observed in 8 cases. The UGIE and colonoscopy were normal study in all these patients. Bone marrow study revealed megaloblastic erythroid hyperplasia. One patient was diagnosed as Aplastic anemia, one as MDS (myelodysplastic syndrome) and 1 remained unexplained

Etiology of Normocytic normochromic type

Normocytic normochromic were observed in 53 patients out of total 100 cases. Causes are shown in Table 1.

Table 1. Etiology of Normocytic normochromic anemia

Etiology	No. of cases
Anemia of chronic kidney Disease	32
Anemia of chronic inflammation	10
Malignancy	09
Unexplained	02
Total	53

In present study, anemia due to chronic renal diseases is the most common cause of anemia in elderly patients. Anemia of chronic inflammation was observed in 10 patients. Two patients had active pulmonary tuberculosis in which sputum for acid fast bacilli was positive with raised ESR and positive manteaux test. Four patients had osteoarthritis. Two patients had rheumatoid arthritis with positive rheumatoid factor and anti-ccp antibodies. One patient had hypothyroidism with raised TSH and one patient had acute infection. All these patients had raised levels of ESR and CRP.

Overall etiology of anemia in elderly

After evaluating all patients the etiological spectrum of anemia can be summarised in Figure 2.

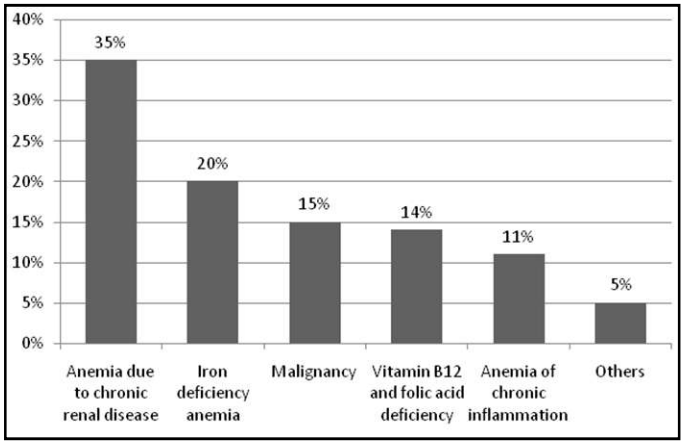

Fig.2. Etiological spectrum of anemia in elderly

As a cause of anemia in elderly patients, malignancy was found in 15 cases. 13 patients were diagnosed as hematological malignancy and 2 patients were diagnosed as non-hematologicalmalignancy. Out of 13 patients, 3 patients were diagnosed as Myelofibrosis, 2 patients were diagnosed as Multiple Myeloma, 2 patients were diagnosed as CML (Chronic Lymphoid Leukemia), 2 patients were diagnosed as CLL (Chronic Lymphoid Leukemia), 1patient was diagnosed as NHL (Non-Hodgkin's Lymphoma), 2 patients had AML (Acute myeloid leukemia). 1 patient was diagnosed as MDS (myelodysplastic syndrome). Bone marrow study revealed increase reticulinfibres with decreased cellularity in myelofibrosis, hypercellular marrow with dysplastic changes in MDS patient, Abnormal plasma cells > 60% in multiple myeloma patient, predominant Lymphocytic precursors in CLL, predominant myeloid precursors in CML.

DISCUSSION

Most of the patients in our study were male. Other studies also reported male preponderance. The most common symptom of generalized weakness, easy fatiguability and most common manifestation of pallor on clinical examination are comparable with the study of Amit Bhasin *et al*. (2011), Saurabh R Shrivastava *et al*. (2013) and Prakash *et al*. (2015). The morpphological pattern of anemia is comparable with other Indian and some international studies however the percentage of patient in each group showe quite difference. In present study, anemia due to chronic renal diseases is the most common cause of anemia in elderly patients followed by Iron deficiency anemia, followed by malignancy that are comparable to study by Amit Bhasin *et al*. (2011). Most of the cases of chronic renal disease had multifactorial etiology, among this diabetes mellitus and hypertension were the most common causes that lead to development of nephropathy in these patients. Most common cause of anemia in elderly in our study is chronic blood loss from GIT followed by underlying GIT malignancy and nutritional deficiency. These findings were again comparable to study by Amit Bhasin *et al*. (2011). In few patients, underlying cause of iron deficiency anemia could not be determined. In present study the third most common cause was in which hematological malignancies were more common which was found in 15% of patients which was comparable with studies by Amit Bhasin *et al*. (2011) and Prakash *et al*. (2015) where incidence of malignancy were 14% and 18% respectively. So, to summarize the hematological causes were 50% and non-hematological causes were 46% and four were unexplained anemia. In our present study the fourth most common cause was Vitamin B_{12} and folic acid deficiency (14%) but as mentioned in Amit Bhasin *et al*. (2011) the exact prevalance of vitB12 and folic acid deficiency is much higher in elderly and is sometimes difficult to detect. In NHANES III study (Woodman *et al*., 2005; Andrès *et al*., 2004) one third of patients were attributed to nutritional deficiency, in another one third due to chronic disorders including chronic kidney disease and in remaining one third cause was unexplained. The cause of anemia in elderly due to chronic kidney disease was 35% (approximately one third), combined iron and vitamin B12 and folic acid deficiency was 34%(approximately one third) i.e. nutrition deficiency and the rest one third malignancies and other miscellaneous causes was present. So, from this aspect our study was also comparable with NHANES III study but in present study unexplained anemia was not so prevalant. The limitation of our study is that many patients referred after taking treatment or blood transfusion for long time from

outside because of that some investigations were remain inconclusive. The major confounding factor is that being a tertiary care centre many patient reporting here were referral patients with chronic diseases and other severe comorbidities that definitely affects the result of our study.

Conclusion

This study of 100 elderly patients of age more than 60 years was conducted to evaluate the etiology and characteristics of anemia. Some patients remain undiagnosed because of paucity of some specific investigations in our institute but still the early categorisation and further specific evaluation was the very important aspect of this study to help in making early diagnosis and management of patients. There are some studies conducted on etiology and some on characteristics of anemia in elderly but few are there that shows complete etiological and morphological evaluation that we have done in this study.

The pattern of anemia (normocytic normochromic followed by microcytic hypochromic followed by macrocytic) is comparable to other Indian studies and most of the international studies but the etiological spectrum vary in between them. However, in the western studies there were more cases of unexplained anemia. The difference could be explained by difference in geographical pattern of chronic disease, patient selection and study design.

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