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Role of serum ferritin in differential diagnosis of anaemia along with various indices of anaemia and their haematological profile in geriatric population.

Anil Raina[1], Suruchi Gupta[2]

[1]Pathologist, District Hospital, Kathua, Jammu and Kashmir.
[2]Pathologist, Gandhi Nagar Hospital, Jammu.

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ABSTRACT

Background: Anaemia is one of the commonest hematological disorders prevalent in elderly population of either sex. WHO suggested any condition with decline of haemoglobin is considered as anaemia. Ferritin an iron storage compound is considered as a well known marker of iron storage. Therefore the present study was designed to evaluate the role of serum ferritin in differential diagnosis of anaemia along with various indices of anaemia and their haematological profile in geriatric population. **Methods:** Complete blood count included the following: Hb level; and white cell indices such as total leucocyte count (TLC) and differential leucocyte count, as well as corrected TLC. All investigations were carried out on an automated cell counter. Serum ferritin was estimated by automated analyser. **Results:** The nutrition deficiency anaemia (47.5%) was most common type of anaemia among elderly population. Further, anaemia due to chronic disease (20.2%), Marrow infiltration (8.3%) and multiple myeloma (7.1%) were recorded in the elderly population. serum ferritin level was significantly low in iron deficiency anaemia (151±88 ng/ml) compare to other types of anaemia dual defficency anaemia (157±98 ng/ml). However, ferritin was significantly high in megaloblastic anaemia (210±101 ng/ml) and anaemia of chronic diseases (204±102 ng/ml). **Conclusion:** Findings of the current study revealed that ferritin can be an important marker for the differential diagnosis of anaemia in elderly population. Moreover, the diagnostic accuracy may be enhanced when PBF and bone marrow findings are combined with clinical examination and other relevant investigations. Biochemical investigation of serum ferritin along with other findings might be helpful in early diagnosis along with accurate aetiology of anaemia in elderly population.

Keywords: Geriatric population, Serum ferritin, Diagnosis, IDA.

INTRODUCTION

Anaemia is one of the commonest hematological disorders prevalent in elderly population of either sex. Prevalence of anaemia has been found higher in geriatric population compare to younger population.[1] Aging is a continuous process which leads to deterioration of various body functions including haematopoiesis especially in elderly subjects.[2] Different types of changes have been shown by peripheral blood picture with decrease of haemoglobin.[3] WHO suggested any condition with decline of haemoglobin is considered as anaemia.[4] Ferritin an iron storage compound is considered as a well known marker of iron storage.[5] Deficiency of haemoglobin may lead to poor quality of life along with increased risk of mortality. Various types of anaemia have been found prevalent in different age groups subjects. Predominantly, anaemia due to nutritional deficiencies and chronic diseases are more commonly found in elderly population.[6,7] Differential diagnosis of anaemia can be made via haematological profile along with various other laboratory findings.[8] Early diagnosis of anaemia in elderly population may help in improving general health and quality of life.[9] Using the different indices of RBC and blood picture along with ferritin level may help to reach the exact diagnosis of anaemia.[10] Therefore the present study was designed to evaluate the role of serum ferritin in differential diagnosis of anaemia along with various indices of anaemia and their haematological profile in geriatric population.

Name & Address of Corresponding Author
Dr. Suruchi Gupta,
Pathologist,
Gandhi Nagar Hospital,
Jammu.

MATERIALS AND METHODS

Study design

In a Tertiary Care Hospital a total of 168 geriatric patients of age 65 years and above, male and female patients with geriatric level anaemia (Hb < 12 g/dl) admitted, were included in the study. Among these patients 92 were male and 76 were female patients.

Informed and written consent from these patients was taken from the patients after explaining them the importance of study. A thorough physical and systemic examination, clinical history, family history, drug history and history of chronic diseases were documented before going for detailed relevant investigations.

The haematological investigations with supporting biochemical parameters were estimated, which included complete blood count, serum ferritin test, peripheral blood film examination, iron studies, serum B12 and folic acid levels, bone marrow cytology, liver and renal function tests, urine examination and radiological examination, when required.

Complete blood count included the following: Hb level; and white cell indices such as total leucocyte count (TLC) and differential leucocyte count, as well as corrected TLC. All investigations were carried out on an automated cell counter (XS-800i63591Analyse APL00-13; Sysmex Corporation, Kobe, Japan).[11] The erythrocyte sedimentation rate (ESR) was determined using Westergrens method and the differential leucocyte count in the case of morbid conditions like leukaemia was confirmed using Leishman's stain and subsequently studied under a microscope using an oil immersion lens.[12]

Serum ferritin was estimated by automated analyser. Serum vitamin B12 and folic acid levels were estimated by means of the Cobase-411 (HITACHI) automated analyser. While, urine examination, including routine, microscopic and examination for Bence Jones proteins, was also carried out to investigate for multiple myeloma.[12] Liver function tests and renal function tests were performed using Siemens Dimension AR automated analyser.

Bone marrow examination

Bone marrow aspiration, trephine biopsy, marrow section and staining of slides were carried out following standard protocol.[11]

Radiological investigations

Radiography of the chest, flat bones and skull, ultrasonography of abdomen, computed tomographic scan and MRI were carried out when required.

Other investigations

The patients were investigated thoroughly to diagnose the underlying disease. This included endoscopy of the upper GIT, mammography, prostatic specific antigen estimation and serum rheumatoid factor.

RESULTS

It is evident from [Figure 1] that nutrition deficiency anaemia (47.5%) was most common type of anaemia among elderly population. Further, anaemia due to chronic disease (20.2%), Marrow infiltration (8.3%) and multiple myeloma (7.1%) were recorded in the elderly population.

[Figure 2] shows that serum ferritin level was significantly low in iron deficiency anaemia (151±88 ng/ml) compare to other types of anaemia dual defficency anaemia (157±98 ng/ml). However, ferritin was significantly high in megaloblastic anaemia (210±101 ng/ml) and anaemia of chronic diseases (204±102 ng/ml).

Further, serum ferritin was observed in marrow infiltration (187±110 ng/ml), multiple myeloma (178±93 ng/ml), myelodysplastic syndrome (187±89 ng/ml), myelofibrosis (176±104 ng/ml), acute myloid leukaemina (183±95 ng/ml), anaemia due to renal disorder (172±76 ng/ml) and chronic lymphocytic leukaemia (178±106 ng/ml).

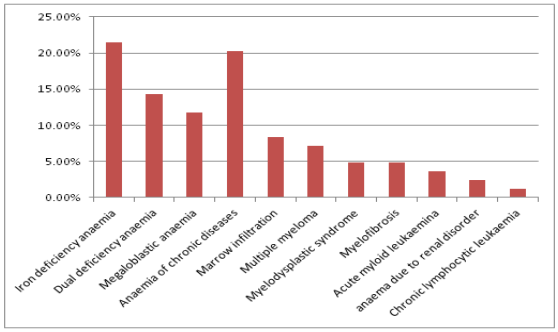

Figure 1: Prevalence of different types of anaemia.

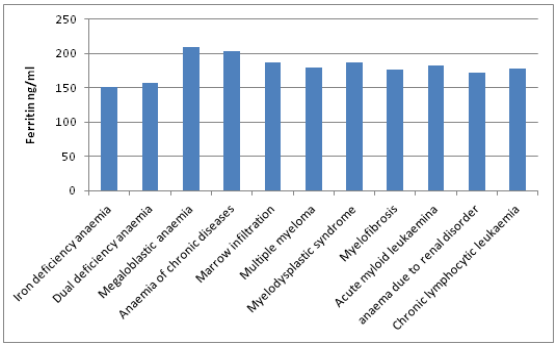

Figure 2: Serum ferritin level in elderly patients.

Table 1: Total leukocyte counts (TLC) in elderly patients.

Total leukocyte count per cumm	No. of patients	Percentage
Normal (4000-11000)	96	57.1
Increased (>11000)	44	26.2
Decreased (< 4000)	28	16.7
Total	168	100

Results further revealed that total leukocyte count varied from 3,000 to 54,000/ cu mm; however, in majority of patients count was within normal range. Increased count was recorded in patients suffering with various other diseases like infectious diseases, leukemia and MDS. Reduced TLC was observed in 28 patients out of which 16 had severe megaloblastic anaemia and metastatic carcinoma in bone marrow. [Table 1]

Table 2: ESR value in elderly patients.

ESR in mm 1st hour	No of patients	Percentage
10-50	56	33.3
51-100	72	42.9
>100	40	23.8

ESR was found raised in all the patients. In 40 patients it was markedly raised (more than 100 mm in 1' hour). These included cases of multiple myeloma, metastatic marrow disease, carcinoma. acute leukemia and tuberculosis. The highest value of 180 rnm in the 1st hour was seen in a patient of multiple myeloma. Majority of elderly patients with anaemia had an ESR in the range of 51 to 100 mm in the 1st hour. [Table 2]

DISCUSSION

The present study has recorded the haematological profile of 168 elderly patients with anaemia to establish the diagnosis and evaluate the role of serum ferritin in the diagnosis of anaemia. Previous studies suggested that appearance of anaemia in elderly subjects is a physiological process and due to advance aging.[2,3] However, recent studies showed that various underlying causes are found for the anaemia which has been found associated with poor outcome in elderly patients.[13,1]

Moreover it is important to investigate anaemia in the elderly. In addition to anaemia, elderly patients are frequently confronted with other medical conditions like heart failure. Ezekowitz JA et al,[14] demonstrated that anaemia is a common and independent prognostic factor in patients with heart failure. Kosiborod M et al,[15] in their studies suggested that anaemia could adversely affect the cardiovascular function of patients with heart failure and yet, the prognostic importance of this treatable condition was not well established by epidemiologic studies. Further, it was concluded that haemoglobin level was an independent predictor of 1-year mortality and of hospital readmission in patients with heart failure. Lower haemoglobin level was associated with a higher mortality. Denny SD et al,[16] have demonstrated deterioration in cognition levels with the fall in haemoglobin levels. In addition, Culletion BF et al,[17] observed in their study that lower haemoglobin level was associated with a higher mortality risk. Pennix BW et al,[15] in their study concluded that anaemia is associated with disability, poor physical performance and lower muscle strength.

Definite clinico-haematological diagnosis in the 168 patients included in the present study was made on the basis of results from clinical examination, routine haematological and biochemical investigations, bone marrow examination and other special investigations. The various underlying pathologies encountered were nutritional deficiency anaemia in 80 (47.6%) patients, anaemia of chronic disease in 34 (20.2%) patients, marrow infiltration in 14 (8.3%), multiple myeloma in 12 (7.1%), myelodysplastic syndrome in 8 (4.8%), myelofibrosis in 8 (4.8%), acute myeloid leukemia in 6 (3.6%), anaemia of renal disease in 4 (2.4%) and chronic lymphocytic leukemia in 2 (1.2%) patient.

Nutritional deficiency anaemia was the most common cause of anaemia in the elderly in our setup especially in residents of old-age homes who were debilitated and not taken care of. Nutritional history of the elderly patients living in old age homes and of those belonging to a lower socio-economic strata revealed that their nutritional status was poor. Their diets were devoid of green leafy vegetables and non-vegetarian foods. Smitha M et al,[19] evaluated the health and nutritional status of 50 elderly living with their families and 50 elderly residing in old age homes. The prevalence of nutritional anaemia was higher in elderly patients (52%). Guralnik JM et al,[1] in their review of NHANES III data, found nutritional deficiency anaemia (blood loss, iron) to be the commonest cause of anaemia in the elderly, accounting for about 34% of the cases. Anaemia of chronic inflammation (ACI) was the other common cause accounting for about 32% of cases. The remaining 34% of the cases were of unexplained anaemia which likely included myelodysplastic syndrome and other miscellaneous causes.

Among the causes of nutritional deficiency anaemia, iron deficiency was the commonest, observed in 36 (21.4%) patients. Majority of the cases of iron deficiency anaemia were due to nutritional deficiency while 16 cases were due to chronic blood loss. Causes of chronic blood loss included two cases of cancer stomach,[2] six patients with stress ulcers and eight patients with haemorrhoids.[6,8] Other causes of nutritional deficiency anaemia included those with dual deficiency in 14.2% of the cases and megaloblastic anaemia in 11.8% of the cases.

These findings are consistent with earlier study of Thomas JH,[20] as they enumerated the various important causes of anaemia in the elderly. These included nutritional deficiency anemias. Myelophthisic anaemia and other causes like renal disease and anaemia of chronic disease. Among the nutritional deficiency anaemia, iron deficiency anaemia was the most common type followed by dual deficiency and megaloblastic anaemia.

Anaemia of chronic disease was the second most common cause of anaemia in the present study and it included cases of pulmonary tuberculosis, rheumatoid arthritis, bronchiectasis, pneumonia and ischaemic heart disease. Anaemia of chronic disease was responsible for anaemia in 17 (20.2%) patients in our study.

These results are very similar to the study of Kirkehy OJ et al 21 as they investigated 72 patients with anaemia aged 70 years and above. Iron deficiency was found in 13 patients and was most often caused by gastro-intestinal blood loss. Chronic disease,

particularly chronic infections and rheumatoid arthritis were responsible for anaemia in 34 patients. Renal failure caused anaemia in 14 patients.

Similarly, Smith DL,[7] found that the common diseases associated with anaemia of chronic disease include chronic infections like tuberculosis, and rheumatoid arthritis. Common causes of anaemia in the elderly in his study were anaemia of chronic disease (45%), iron deficiency (30%), Vitamin B12 and folate deficiency (10%), chronic lymphocytic leukemia (5%) and myelodysplastic syndrome (5%). No identifiable cause could be found in 5% of patients.

Alike, Rimon E et al,[22] demonstrated iron deficiency anaemia was most common on bone marrow aspirates in a prospective controlled study of 49 consecutive male and female patients older than 80 years.

Results of the present study showed that there was significantly decrease level of serum ferritin in iron deficiency anaeima along with nutritional deficiency anaemia compare to other types of anaemia in elderly anaemic patients. The values were very low in iron deficiency anaemia and high in anaemia of chronic disease. Cases of dual deficiency anaemia also showed lower serum ferritin levels. Megaloblastic anaemia cases showed higher serum ferritin levels. Serum ferritin levels were within normal range in cases of multiple myeloma. Serum iron levels were reduced in both iron deficiency anaemia and anaemia of chronic disease.

These findings are in agreement with the findings of the earlier study of Milman N et al,[23] as they recorded significant decrease of serum ferritin level in Danish people of more than 80 years age group. Similarly, Coenen JL et al,[24] observed a significant decrease in serum ferritin level in anaemic patients compared to control. Alike, Kis A et al,[25] showed that ferritin level was significantly low in IDA. In addition, Thomas JH,[20] recorded in their study that decrease of serum ferritin along with presence of microcytic hypochromic red cell population and low mean corpuscular volume (MCV) favors the diagnosis of iron deficiency anaemia.

Smiejaet at,[26] investigated 186 patients of iron deficiency anaemia in their study and found that serum ferritin level is one of the most important investigations for arriving at the diagnosis. Serum ferritin level was consistently found to be less than 18 µg/litre in patients of iron deficiency anaemia. Guyatt et al,[27] in their study remarked that a low serum ferritin level of < 45 µg/litre diagnosed iron deficiency anaemia in elderly patients with anaemia. They concluded that serum ferritin level estimation was the most powerful test for the diagnosis of iron deficiency anaemia.

Smith DL,[7] in his article mentioned that serum ferritin is the most useful test, differentiating anaemia of chronic disease from iron deficiency anaemia in 70 percent of patients. The serum ferritin level is the most effective way to diagnose iron deficiency anaemia. When the serum ferritin is less than 15 µg/litre, iron deficiency is virtually certain. Iron deficiency is unlikely if the serum ferritin level is greater than 100µg/litre. Patterson et al,[28] in their study found that serum ferritin level proved to be the most powerful of the laboratory tests for diagnosing iron deficiency anaemia.

The total leukocyte count varied from 3000/cumm to 54,000/cu mm in the present study. Leukopenia was observed in 14 patients; of these 8 patients were of severe megaloblastic anaemia, 2 were of acute leukemia and 4 were of metastatic marrow disease. Increased leukocyte count was observed in patients suffering from various infectious diseases like pneumonia, bronchiectasis and in cases of malignancy. Smith DL,[7] in his review article stressed upon the need to determine TLC in the initial evaluation of anaemia in the elderly. He found abnormal WBC counts in most of his patients with leukemia and MDS. He mentioned that pancytopenia is an important indication for bone marrow aspiration or biopsy.

ESR values were elevated to upto 100 mm in first hour in patients of anaemia of chronic disease while ESR values were observed to be elevated up to 150mm in first hour in patients of carcinomatous marrow disease. Maximum value of 180 mm in first hour was observed in a patient of multiple myeloma. Beutler E,[29] in their study pointed to the importance of elevated ESR as an indication of some underlying disease.

CONCLUSION

Findings of the current study revealed that nutritional deficiency anaemia was most common among elderly population. Increase of ESR was common in all elderly anaemic patients. However, decreased TLC was found in megaloblastic anaemia. Further, results of the present study suggest that ferritin can be an important marker for the differential diagnosis of anaemia in elderly population. Moreover, the diagnostic accuracy may be enhanced when PBF and bone marrow findings are combined with clinical examination and other relevant investigations. Biochemical investigation of serum ferritin along with other findings might be helpful in early diagnosis of anaemia in elderly population.

REFERENCES

1. Guralnik JM, Eisenstaedt RS, Ferrucci L, Klein HG, Woodman RC. Prevalence of anemia in persons 65 years and older in the United States: evidence for a high rate of unexplained anemia. Blood 2004; 104:2263–2268.
2. Gualandro SF, Hojaij NH, Jacob Filho W. Deficiência de ferro no idoso. Rev Bras Hematol Hemoter. 2010;32(supl. 2):57-61.
3. Mukhopadhyay D, Mohanaruban K. Iron deficiency anaemia in older people: investigation, management and treatment.

Age Ageing. 2002;31(2):87-91. Comment in: Age Ageing. 2003;32(1):116-7.
4. De Benoist B, McLean E, Egli I, Cogswell ME, editors; World Health Organization (WHO). Worldwide Prevalence of Anaemia 1993–2005: WHO Global Database on Anaemia. Geneva, Switzerland: WHO; 2008.
5. Lipschitz DA, Cook JD, Finch CA. A clinical evaluation of serum ferritin as an index of iron stores. N Engl J Med: 1974; 290:1213-1216.
6. Sánchez H, Albala C, Hertrampf E, Verdugo R, Lavados M, Castillo JL, et al. [Prevalence of vitamin B-12 deficiency in older adults]. Rev Med Chile. 2010;138(1):44-52. Spanish.
7. Smith DL. Anemia in the elderly. Am Fam Physician. 2000;62(7):1565-72.
8. Mukhopadhyay D, Mohanaruban K. Iron deficiency anaemia in older people: investigation, management and treatment. Age Ageing. 2002;31(2):87-91. Comment in: Age Ageing. 2003;32(1):116-7.
9. Paiva AA, Rondó HC, Shinohara EM. [Parameters for the assessment of iron status] Rev Saude Publica. 2000;34(4):421-6. Portuguese.
10. Wintrobe, MM. Hematologia Clínica. Manole: São Paulo: 1998.
11. Dacie JM, Lewis SM. Practical haematology. 9th ed.. New York: Churchill Livingstone Publication; 2001.
12. Sood R. Medical laboratory technology: methods and interpretation. 5th ed. New Delhi: Jaypee Brothers Medical Publishers; 1999.
13. Smith DL. Management and treatment of anemia in the elderly. Clinical Geriatrics. 2002;10(8):47-53.
14. Ezekwitz JA, McAlister FA, Armstrong PW. Anemia is common in heart failure and is associated with poor outcomes: insights from a cohort of 12 065 patients with new-onset heart failure. Circulation. 2003;107(2):223-5.
15. Kosiborod M, Smith GL, Radford MJ, Foody JM, Kruholz HM. The prognostic importance of anemia in patients with heart failure. Am J Med. 2003;114(2):112-9.
16. Denny SD, Kuchibhatla MN, Cohen HJ. Impact of anemia on mortality, cognition, and function in community-dwelling elderly. Am J Med. 2006 Apr;119(4):327-34.
17. Culleton BF, Manns BJ, Zhang J, Tonelli M, Klarenbach S, Hemmelgarn BR. Impact of anemia on hospitalization and mortality in older adults. Blood 2006 107:3841-3846.
18. Penninx BW, Pluijm SM, Lips P, Woodman R, Miedema K, Guralnik JM, Deeg DJ. Late-life anemia is associated with increased risk of recurrent falls. Am Geriatr Soc. 2005;53(12):2106-11.
19. Smitha M, Devi NL. Health and nutritional status of free living and institutionalized elderly in Chittoor District. Journal of Research ANGRAU 33(2): 42-46.
20. Thomas JH. Anaemia in the elderly. Br Med J. 1973 Nov 3;4(5887):288-90.
21. Kirkeby OJ, Fossum S, Risoe C. Anaemia in elderly patients. Incidence and causes of low haemoglobin concentration in a city general practice. Scand J Prim Health Care. 1991 Sep;9(3):167-71.
22. Rimon E, Levy S, Sapir A, Gelzer G, Peled R, Ergas D, Sthoeger ZM. Diagnosis of iron deficiency anemia in the elderly by transferrin receptor-ferritin index. Arch Interl Med. 2002 Feb 25;162(4):445-9.
23. Milman N. Anemia--still a major health problem in many parts of the world! Ann Hematol. 2011 Apr;90(4):369-77.
24. Coenen JL, van Dieijen-Visser MP, van Pelt J, van Deursen CT, Fickers MM, van Wersch JW, Brombacher PJ. Measurements of serum ferritin used to predict concentrations of iron in bone marrow in anemia of chronic disease. Clin Chem. 1991 Apr;37(4):560-3.
25. Kis A, Carnes M. Detecting iron deficiency in anemic patients with concomitant medical problems. J Gen Intern Med. 1998; 13 (7): 455-61.
26. Smieja MJ, Cook DJ, Hunt DL, Ali MAM, Guyatt GH. Recognizing And Investigating Iron-Deficiency Anemia In Hospitalized Elderly People. CAN MED ASSOC J, 1996;155 (6)25.
27. Guyatt GH, Patterson C, Ali M, Singer J, Levine M, Turpie I, Meyer R. Diagnosis of iron-deficiency anemia in the elderly. Am J Med. 1990;88(3):205-9.
28. Patterson C, Guyatt GH, Singer J, Ali M, Turpie I. Iron deficiency anemia in the elderly: the diagnostic process. CMAJ. 1991 Feb 15;144(4):435-40.
29. Beutler E, Waalen J. The definition of anemia: what is the lower limit of normal of the blood hemoglobin concentration? Blood; 2006 107: 1747-1750.

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