Chapter

Geriatric Anemia

Manjit Kaur Rana and Amrit Pal Singh Rana

Abstract

Anemia is growing in importance as a public health issue and a biomedical research priority in the geriatric age group but data on the causes and prevalence is not substantial. World health organization (WHO) has defined anemia as hemoglobin concentration (Hb %) below 12 g/dL in women and below 13 g/dL in men. Although it was previously believed that decline in Hb levels might be a normal consequence of aging, later suggested that anemia does reflect underlying poor health and makes elders vulnerable to adverse outcomes. Geriatric anemia has been found to be prevalent in up to 21.1% of patients in Europe and 11.0% of men and 10.2% of women of 65 years and older in the US. There is little literature that explores the various causes of anemia and its association with socio-demographic profile with underlying diseases, hence lesser research has led anemia to go undiagnosed and untreated.

Keywords: geriatric, generalized weakness, unexplained anemia

1. Introduction

Anemia is rising in importance as a biomedical research priority and a public health issue in the old age group. World health organization (WHO) has defined anemia as hemoglobin concentration (Hb %) below 12 g/dL in women and below 13 g/dL in men [1]. Hb declines slightly with more advancing age with frequency of anemia being more pronounced in men. The geriatric anemia is related with mortality and inferior health associated quality of life [2, 3]. This is important area to be explored as there is little literature that explains the association of anemia with old age and lesser research has led anemia to go undiagnosed and untreated. In the shade of absent obvious ailment, complaints of generalized weakness left ignored [4–9]. The incidence of anemia increases comorbidities resulting in increased frequency of hospitalizations hence leading on to adverse impact on survival [10, 11]. So a better outlook is needed to define the optimal Hb levels and to diagnose out the cause of anemia in old age group [12, 13].

2. Definition of anemia and epidemiology

The definition of anemia in the elderly in the literature is controversial. The WHO criteria were established in the 1960s in a cohort lacking individuals >65 years of age [14]. According to WHO criteria anemia was defined as hemoglobin <12 g/dL in women and <13 g/dL in men and absolute iron deficiency was defined as a serum ferritin <30 ng/mL [15, 16]. The National Health and Nutrition Examination Survey

III classifies anemia into four categories as per underlying cause such as anemia from nutritional deficiency, anemia due to renal diseases, anemia of chronic disease and unexplained anemia, in the absence of other specific causes. Worldwide both the number and ratio of older adults growing and there are nearly 500 million (7%) adults, 65 years and older in the world and by 2030 will double to 1 billion (12%). It was predicted that 164 million elderly people who constitute 23.9% of geriatric population were suffering from anemia globally and death risk was elevated to 49% [3, 17]. As per a systematic review the prevalence of anemia was found to be 3–50%. Out of that 3–25% constituted from community-based studies, 31–50% from nursing homes studies and 40–72% hospital admissions [18]. The prevalence of anemia in the institutional studies was observed to be 24%, 31.4%, 46.8%, 54.5%, 66.3%, 67% and 74% in Belgium, Israel, Pakistan, Ethiopia, German, China and US Arespectively [1, 19–23]. Whereas the prevalence of anemia was observed to be 7.3%, 17.7%, 19% and 38% in Turkey, rural India, Iran and urban India respectively in population-based studies [24–27].

3. Clinical features

In elderly, anemia is ignored frequently in spite of obvious evidence that due to decreased Hb levels physiologic functions may worsen in the patients [28]. It has been noticed that there are 75% chances of negligence of symptoms by the patients [29, 30]. Also no related positive finding could be recognized on general physical examinations as there are insufficient signs on physical examination that are specific for mild to moderate anemia [3, 31, 32]. However signs and symptoms vary from weakness, irritability, alopecia, xerostomia and depression especially in iron deficiency anemia (IDA). The restless leg syndrome seen in elderly is also commonly take place with iron deficiency [33–35]. Many studies searched in literature verified that anemia is an independent risk factor for rise in morbidity and mortality along with decreased quality of life in older persons [18, 28, 36–38].

4. Etiopathogenesis

Geriatric anemia to a certain extent may be due to unrevealed underlying diseases or due to reduced bone marrow functional reserve or adaptation to reduced lean body mass with diminished oxygen requirements or escaped erythropoietin secretions. There is plenty of substantiation that hematopoietic stem cells undergo some qualitative changes with age hence resulting in reduced proliferative and regenerative capacity. It has been realized that anemia at older age is rising with the possibly of changes in diagnostics and demographics. Though this also have been emphasized by authors that anemia in the elderly do has a treatable cause [18, 39, 40]. The etiopathogenesis of anemia in geriatric age group is multifaceted and varying from nutritional deficiencies to inflammatory progressions resulting in immunodeficiency. Other causes may be from bone marrow failure syndromes to chronic kidney disease. In general causes of anemia were found to be anemia of chronic disease (ACD) associated with co morbidities, deficiency anemia constituting iron deficiency, vit B 12 deficiency, folate deficiency and others and unexplained anemia. While considering the underlying diseases, anemia in elderly is also seen associated with *H. pylori* and twice prevalent in people with chronic kidney disease (CKD), withprevalence of anemia increasing with stage of CKD [22, 33, 41, 42]. Under normal circumstances, increased plasma and stored iron levels activate Hepcidin production, a hormone released by liver which in turn inhibits

dietary iron absorption. Anemia due to iron deficiencies can occur due to low iron content in diet, decreased iron uptake by intestine or excessive bleeding, and compensated by increased erythropoiesis. IDA seemed to be associated with obesity, gastritis and peptic ulcer, esophagitis, Crohn's disease, celiac disease etc. Although, polymedication was considered independent risk factor for anemia, a 12–35% higher chance of anemia was seen in aspirin users alone. Other drugs like corticosteroids and anti-acids were also seen associated with IDA [43, 44]. Screening for under nutrition should be included in assessment of anemia in geriatric patients as low serum albumin levels are found as independent risk factors for anemia in geriatric patients [44, 45]. The association of deficient serum vitamin D levels with anemia is not considered significant as hypoalbuminemia is measured likely to be confounding factor. At the same time as considering the sociodemographic profile as a causative factor, geriatric anemia was significantly seen associated with high socioeconomic status followed by employment and chronic diseases [45, 46]. Another aspect discussed by Freedman ML and associate suggested that low values in elderly especially in men is a physiologic phenomenon or values of anemia need to be revised in this age group is not known [31, 47].

5. Types of anemia

As per National Health and Nutrition Examination Survey III anemia has been classified into four categories as per underlying cause such as anemia from nutritional deficiency, anemia due to renal diseases, anemia of chronic disease and unexplained anemia, in the absence of other specific causes.

Anemia of chronic disease (ACD) is found to be the most common cause of anemia. The prevalence of ACD varies from 33.1–77% in elderly patients (**Table 1**) [1, 37, 48].

The cause of ACD in hospitalized elderly patients is mostly the consequence of added chronic underlying diseases and also is an indicator of several reactive and clonal conditions.3 Many underlying diseases, like H pylori, renal impairment, congestive heart failure, myelodysplastic syndrome (MDS) is seen associated with ACD in elderly [19, 42, 51]. Although concentrations of serum ferritin, white blood counts (WBC) and C-reactive protein (CRP) levels in ACD patients remains high in ACD but high Hepcidin (H) level occurring due to inflammation facilitates development of ACD in elderly patients. Wang WJ et al. have emphasized that best threshold value for the diagnosis of ACD is 130.05 μg/L with the sensitivity of 72% and the specificity of 96% [51–53]. An analysis done by López-Sierra Metal also favored use of serum Transferrin Receptor (sTfR) to check out the state of erythropoiesis in patients with chronic disease [54].

Prevalence	Author's name, year
35%	Joosten E et al., 1992 [1]
65.6%	Chernetsky A et al., 2002 [19]
64%	Willems JM et al., 2012 [49]
77%	Joosten E et al., 2014 [48]
46%	Gowanlock Z et al., 2016 [50]
33.1%	Michalak SS et al., 2018 [37]

Table 1.
Prevalence of anemia of chronic disease in geriatric age group.

Nutritional deficiency anemia is an important clinical problem with prevalence varying from 4% to 22.5% in older patients associated with caloric and protein restriction, iron, vitamin B12, folic deficiency [19, 37, 48, 55]. Protein and energy malnutrition cause an increase in the production of cytokine, stimulation of inflammationand anemia. Due to decreased macrophages activity and ineffective erythropoiesis, reduced red cell mass is seen. In addition, increased cytokines and hepcidin serum levels also seen associated with obesity and underweight [56]. Anemia patients with protein and energy malnutrition more frequently suffered from hypoalbunemia [43]. Absolute IDA is well-defined as anemia with absence of total body iron. To diagnose IDA although serum ferritin is the most often used parameter, but with older age and in the presence of inflammatory diseases concentration of serum ferritin increases and losses its significancy.10Iron deficiency anemia (IDA) contributes approximately 13–15% of total anemia of geriatric age group, mainly associated with underlying diseases.Evidence has been supported by improvement of IDAfrom iron rich diet in geriatric patients [1, 37, 48, 55, 57–59]. New insights into iron homeostasis lead to new diagnostic assays such as serum baseline hepcidin levels could be a useful tool to identify ID in anemic elderly patients. Wang WJ et al. have highlighted thatthe best threshold in diagnosis of IDA was 93.31 μg/L with the sensitivity of 88% and the specificity of 89% [53, 54, 60, 61]. In addition serum transferrin receptor and reticulocyte hemoglobin equivalent is also an emerging investigation to diagnose the disease [54].

Anemia due to CKD fall under the category of decreased RBC production and prevalence varies from 13.2–27% of geriatric anemia [19, 49]. In a smaller number of cases, no clear-cut causes of anemia are identified and when a clear etiopathogenesis is ruled-out the anemia is defined as unexplained anemia (UA) term unexplained anemia. Although the reasons are still under-explored but common pathophysiological mechanisms seems to be associated with an age-related inflammatory process [62, 63]. These patients with unidentified causes are referred to as unexplained anemia or idiopathic cytopenia of unknown significance. The erythropoietin genesis in the kidney becomes suboptimal due to age related affects or changes. This aspect is still underestimated and unexplored while dealing with unexplained anemia. The prevalence of UA varies from 5.8% to 43.7% of the cases (**Table 2**). Many researchers have worked on UA, Price EA and fellows have observed mildly increased inflammatory markers and low erythropoietin levels in patients with this entity. Roy CN and associates have observed that testosterone treatment in case of men 65 years or older with UA and low testosterone levels significantly increased the hemoglobin levels. In testosterone trials, testosterone treatment increased Hb levels in both men who had anemia of a known cause and in men with UA [3, 37, 61, 64–66]. However, similar survival was observed in geriatric patients with UA compared with non-anemic subjects but mortality risks was increased in patients with deficiency anemia compared with non-anemic subjects [49]. The erythropoietin levels seen

Prevalence (%)	Authors name, year
36.8%	Ferrucci L et al., 2007 [64]
43.7%	Artz AS et al. 2011 [23]
35%	Willems JM et al., 2012 [49]
5.8%	Wolff F et al., 2018 [61]
28.4%	Michalak SS, et al., 2018 [37]

Table 2.
Prevalence of unexplained anemia.

inappropriately low in UA indicating that decreased erythropoietin production plays an important role in the pathogenesis of anemia of unknown etiology [50]. On further cytogenetic analysis of UA, one researcher found myelodysplastic syndrome in 4% of the total anemic patients [67]. Whereas in others, present somatic mutations were not found fit as per diagnostic criteria for MDS and condition was termed as clonal cytopenia of undetermined significance [68].

6. Microscopic patterns of anemia

Normocytic anemia being the commonest anemiafollowed by microcytic hypochromic and macrocytic as studied by Kim HS et al. The most common pattern of anemia in a study done by Choi CW has been found to be normocytic anemia amounting to 93.5%, and 3.5% of them being microcytic, and 3% were macrocytic anemias. Bhasin A et al. study showed that most common pattern of anemia as normocytic in 60–90 years age group [69–71].

7. Grade of anemia

WHO classified anemia as public health problem in 2008 into mild, moderate and severe category [72]. Most common grade appreciated is mild (57.1%) with mild to moderate anemia commonly affecting females.While severe and life-threatening anemia is confronted in males predominantly [73]. As greater part of the patients are mild anemia only, foremost findings are difficult to observe even pale conjunctiva usually noted when Hb level drops below 9 gm/dL [32]. So this may be the reason that patients of this grade go unnoticed. For example in a study conducted on 1,146 community-dwelling older females it was found that women with Hb levels of 12 to 13 gm/dL perform worse than women with Hb levels of 13 to 15 gm/dL on tests of walking speed, balance and ability to raise from a chair [74]. Across-sectional study including 334 elderly persons was conducted by Pathiana A and fellows in old age home. The overall prevalence of anemia was found to be 68.7%, 47.4% had mild anemia, 47.0% had moderate anemia and 5.6% had severe anemia with 45% of men with mild anemia as compared to 24.8% in women [30].

It has been suggested in the literature that a diagnostic algorithm should be followed and anemia should be classified with a therapeutic orientation. Supplements of iron, micronutrients and erythropoiesis-stimulating agents should constitute the treatment [75].

8. Conclusion

Anemia in older people is typically mild so it is likely to be overlooked. All elderly persons presenting with health issues should be evaluated for anemia first with complete list of parameters. Proportion and pattern of anemia should be confirmed so that overall outcome and quality of life in case of old age can be improved with specific treatment. Future population-based research is essential for refining for diagnostic testing to tackle out the etiology of geriatric anemia and evaluate effective therapies to reduce the disease burden on the society.

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