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Research Article

Favorable Hematological Profile of the Oldest Old Residents from South Central United States -

Krishna P. Joshi, Priya Priyambada, Amanda Pangle, Jeanne Y. Wei, and Gohar Azhar*

Reynolds Institute on Aging, University of Arkansas for Medical Sciences, USA

***Address for Correspondence:** Gohar Azhar, Reynolds Institute on Aging, University of Arkansas for Medical Sciences, Little Rock, AR 72205, USA, Tel: + 501- 686-5884; E-Mail: azhargohar@uams.edu

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ABSTRACT

We conducted a retrospective study of 178 community dwelling elderly on anemia which was defined as hemoglobin < 13 gm/ dl in males and < 12 gm/ dl in females (WHO guidelines).

Methods: This was a retrospective chart review of patients aged ≥ 95 years, who were seen over a two year period at the University of Arkansas for Medical Sciences.

Results: The mean age of the patients was 97 ± 2.7 years (range, 95 - 112). Sixty-five percent were White, 32% African Americans, and 3% Hispanic or other ethnicities. Approximately 60% of patients were anemic with mean hemoglobin of 11.8 ± 1.92 gm/ dl. The prevalence of anemia was higher in the African Americans (69%) versus the White, non-Hispanic (56%), although there was no significant difference in the degree of anemia between the two groups (hemoglobin: 11.4 ± 1.8 vs 11.8 ± 1.8). Approximately 60% of the anemias were normocytic, with microcytic and macrocytic comprising the rest. Serum iron levels were significantly lower in African Americans vs White, non-Hispanics (29.1 ± 7.7 vs 42.9 ± 12.9; $p < 0.05$, t-test). In addition, 35.8% of patients had renal failure, 30% were iron deficient, 11.3% were hypothyroid, and 17% were vitamin B12 deficient. The available data did not suggest any leukemia or lymphomas. However, 7.5% of patients (n = 8) had documented histological evidence of solid tumors.

Surprisingly, approximately 40% of the oldest old were not anemic. Our study population also appeared to have "escaped" clinically significant leukemia and lymphomas. Anemia was more prevalent in the African Americans, as were lower iron levels. More studies are needed to elucidate the underlying molecular mechanisms for the relatively preserved hematological health in this segment of oldest old, which might have contributed to their exceptional longevity.

Keywords: Anemia; Elderly; Oldest old; Longevity

INTRODUCTION

Anemia is a common medical problem in elderly and its prevalence increases with age [1]. The geriatric population is growing exponentially worldwide. Globally, the population aged > 60 years was 8% in 1950 and 12% in 2013, but is estimated to reach 21% by 2050 [2]. The World Health Organization (WHO) has defined anemia as hemoglobin less than 13 gm/ dl in male and 12 gm/ dl in non-pregnant female adults [3]. Although some studies have been done to determine the normal ranges for age and gender associated changes in hemoglobin levels, the WHO definition is still the most widely used [4]. However, the WHO criteria is based on studies that did not include data from individuals more than 65 years of age [5]. Nevertheless, some studies have applied the WHO criteria for anemia to the geriatric population and have classified 17% of those over 65 as being anemic. The prevalence of anemia increases with illness and frailty, being 40% in hospitalized geriatric patients and 47% in nursing home residents [6]. Anemia in elderly has been found to be associated with cognitive impairment, cardiovascular disease, decreased physical performance, increased risk of falls and fractures, longer hospital stay, reduced quality of life, and increased risk of mortality [7]. People over the age of 85 are currently the fastest growing age-group and will contribute to the increasing centenarian population in this country [8]. Hence, it is imperative that the healthcare force is better informed about this segment of the population. To this end, we conducted a retrospective study of anemia in nonagenarians and centenarians residing in Arkansas, which is representative of the South-Central part of the United States.

METHODS

This was a retrospective study design, based on review of Electronic Medical Records (EMR) of patients seen at the University of Arkansas for Medical Sciences (UAMS), Little Rock, Arkansas. The study was approved by the Institutional Review Board (IRB) of UAMS, # 201959. A retrospective chart review was conducted for subjects seen at UAMS between January 2011 and June 2013. Patients who were deceased, had moved out of the state, or had no laboratory workup done were excluded from the analysis.

The demographic variables included age ≥ 95, gender, and race/ethnicity. Laboratory data included hemoglobin, serum iron, ferritin, iron binding capacity, folate, vitamin B12, kidney function, and vitamin D level. Data were also mined for other potential contributors of anemia such as thyroid disease, hematological or solid malignancies, and other co-morbid conditions. BMI was used as a general indicator of nutrition and health. Since normative standards for hemoglobin have not been determined in this age group, the WHO values for anemia were employed, with hemoglobin < 13 gm/ dl in males and < 12 gm/ dl in females.

STATISTICS

Approximately 95% of the data were collected from the last available clinic visit of the patient. Some of the patients' visits to the hospital were for subspecialty care, and these data were also included in the analysis. The analyses were performed using SAS software (version 9.3, SAS Institute Inc., Cary, NC). The standard t-test was used and where numbers were small, non-parametric tests such as the Mann-Whitney U or Anova on Ranks were employed. An alpha cut-off of 0.05 was used for significance.

RESULTS

This retrospective study included the chart review of 178 elderly patients, 95 years and older. Out of 178 total patients, 84% were female and 16% male. Mean age of the patients was 97 ± 2.7 years (Table 1). The majority of the patients were White, non-Hispanic, comprising 65% of the studied subjects, with African Americans at 32%, and about 3% Hispanic or mixed origin. There were a greater percentage of women in the African American group with a 1:10 male to female ratio, compared with approximately 1:5 in the White, Non-Hispanic group (Table 1). About 59% of the patients (n = 106) were anemic and 41% had normal hemoglobin values (Table 1).

There was a racial difference with 56% White, non-Hispanic versus 69% of African Americans being anemic (Table 2). We further compared the degree of anemia in the two major racial groups with their demographic characteristics (Table 2). Since there was only 1 Hispanic male in the data set (with a HB of 16.1 gm/ dl), and only five with mixed or unknown ethnicity (mean Hb 13.3 ± 2.3), we did

not include them in the analysis. The mean hemoglobin of the entire anemic cohort was 11.8 ± 1.92 gm/ dl, while that of the White, non-Hispanics and African Americans was comparable, with no significant difference (11.8 ± 1.8 vs11.4 ± 1.8 gm/ dl respectively). There was tendency for a slightly lower BMI in the White, non-Hispanics vs. the African-Americans but the results were not significant. In the majority of patients (61%), the anemia was normocytic, whereas 13.2% had microcytic anemia, 13.2% had macrocytic anemia and an equal number lacked data on mean corpuscular volume. In approximately one-third of patients, no work-up had been conducted to diagnose the underlying etiology of anemia.

We reviewed the data related to potential etiological factors for anemia in the White, non-Hispanic and African American groups (Table 3). Overall, about 35.8% of patients had renal failure, which was almost equally distributed between White, Non-Hispanic and African Americans. The mean serum creatinine was slightly higher in the African Americans at 2.2 ± 0.9 vs 2.0 ± 0.4 for White, Non-Hispanics, but the difference was not significant. Iron studies were available in 30% of anemic patients; serum iron levels were significantly lower in African Americans compared with White, non-Hispanics (29.1 ± 7.7 vs 42.9 ± 12.9, respectively; $p < 0.05$, t-test). Hypothyroidism appeared to affect the White, Non-Hispanics more than the African Americans, but the TSH values were not significantly different between the two groups. Similarly, vitamin B12 deficiency tended to occur with greater frequency in the White, non-Hispanic vs the African Americans with no significant difference between the groups. Furthermore, 13.2% of anemic patients had possible cachexia syndrome with a low BMI ≤ 20, which was more common in White, non-Hispanic patients. The available data did not suggest any leukemia, lymphomas, or other myeloproliferative or dysplastic disorder. However, 3.6% of patients (n = 8) had documented histological evidence of tumors (2 colon, 2 breast, 1 urinary bladder, 1 sarcoma, 1 thyroid, 1 laryngeal) that were distributed between the groups. About 2% (n = 3) of the anemic patients had suffered from documented gastrointestinal bleeds.

We also compared the prevalence of dementia and heart failure and its racial distribution in patients (Table 4). A diagnosis of dementia was recorded in 48.7% of anemic African Americans vs 42% of anemic White, non-Hispanics. Heart failure was noted to be present in 12.8% of anemic African Americans compared to 19.6% White, Non-Hispanics. Overall, anemic patients appeared to have a higher rate of diagnosis of dementia versus non-anemic (44.3 vs. 37.5). Additionally, the diagnosis of heart failure was also higher in anemic versus non-anemic patients (16.9 vs. 11.1).

Table 1: Patient Demographics

Age, gender, and condition	N	%
Total N	178	
Mean Age (SD)	97 (± 2.7)	
Males	28	15.70%
Females	150	84.30%
Patients without anemia	72	40.50%
Patients with anemia	106	59.50%
Race/Ethnicity		
White, non-Hispanic (20 males, 96 females)	116	65.00%
Hispanic white (1 male)	1	0.50%
African American (5 males, 51 females)	56	31.40%
Unknown/mixed ethnicity (2 males, 3 females)	5	2.80%

Table 2: Characteristics of Patients with Anemia

Anemic population	N (% of total)
Total anemic	106 (17% males, 83% females)
White, non-Hispanic	65 (56%)
African American	39 (69%)
Male	18 (64%)
Females	88 (59%)
Characteristics	**Mean ± SD**
Age, White, non-Hispanic	97.1 ± 7.1
Age, African Americans	96.8 ± 5.1
Hb (gm/ dl), All anemic	11.8 ± 1.9
Hb, White, non-Hispanic	11.8 ± 1.8
Hb, African American	11.4 ± 1.8
BMI, All anemic	24.4 ± 4.0
BMI, White, non-Hispanic	23.86 ± 3.5
BMI, African American	25.78 ± 4.2

Table 3: Etiological Factors

	Laboratory values
Renal failure	*S. Creatinine*
White, non-Hispanic	2.06 ± 0.4
African American	2.2 ± 0.9
Iron deficiency*	*S. Iron*
White, non-Hispanic	42.9 ± 6.5
African American	29.1 ± 7.9
Hypothyroidism	*TSH*
White, non-Hispanic	13.3 ± 5.4
African American	10.4 ± 7.44
Vitamin B12 deficiency	*B12*
White, non-Hispanic	271 ± 82
African American	290 ± 73.9
Blood loss, GI bleed	
Cachexia syndrome (BMI < 20)	*BMI*
White, non-Hispanic	19.1 ± 1.6
African American	18.9 ± 0.3
Cancers	
Colon (2 AA)	
Breast (AA + W)	
Thyroid (AA)	
Larynx (W)	
Sarcoma (W)	
Urinary bladder (AA)	

Potential etiological factors in anemia patients. W = White, non-Hispanic; AA=African American; *$p < 0.05$

DISCUSSION

Anemia was defined by WHO in 1968 as hemoglobin < 13 g/ dL in men and < 12 g/ dL in women. However, WHO criteria for anemia was based upon data in populations that did not include individuals > 65 years of age, so the optimal level of hemoglobin in this population is unknown [1-6].

Table 4: Prevalence of dementia and heart failure in patients

African American	N	Dementia, N (%)	Heart failure, N (%)
Anemic	39	19 (48.7)	5 (12.8)
Non-anemic	17	8 (47)	1 (5.8)
Total	56	27 (48.2)	6 (10.7)
White, non-Hispanic			
Anemic	66	28 (42)	13 (19.6)
Non-anemic	50	19 (38)	7 (14)
Total	116	47 (40)	20 (17.2)
All patients			
Anemic	106	47 (44.3)	18 (16.9)
Non-anemic	72	27 (37.5)	8 (11.1)

Several interesting findings emerged from our study of this novel population of the oldest old. Firstly, in spite of the advanced age, approximately 41% of the patients were not anemic. Secondly, although the prevalence of anemia was higher in African Americans compared to White, non-Hispanics, the degree of anemia was mild and comparable between the two groups. Thirdly, iron deficiency was significantly higher in the African Americans versus the White, non-Hispanics. Finally, there was no evidence of hematological malignancies, and only 3% of the subjects had documentation of solid tumors in their records.

Although there are many studies on the prevalence and consequences of anemia in people over 65 years of age, there is a dearth of studies on anemia in nonagenarians and centenarians in literature [5,9,10]. In data from the third US National Health and Nutrition Examination Survey (NHANES III), 26% of men and 20% of women aged ≥ 85 were anemic [11]. In our own study, approximately 64% of men and 59% of women ≥ 95 were anemic. This difference could be because of the advanced age of our population or due to a smaller sample size, regional or genetic variations. A number of studies have reported on the higher prevalence of anemia in African Americans [11-13,16]. Our study had higher percentages of anemic African Americans (69%) and White, Non-Hispanics (56%) compared to the NHANES III data that reported lower numbers of anemic African American (27.8%) and Caucasians (9%) [11,12,16]. However, the lower age limit for the NHANES III study was 65 years, whereas in our study the lower age limit was 95. In addition, approximately one-third of our study population was African American which could explain some of the observed differences. Poverty and a higher co-morbidity burden in African Americans could have contributed to some anemia in our subjects; however other studies have suggested that the lower hemoglobin levels might be related to genetic polymorphisms of sickle cell trait and α-thalassemia [14-16]. In our review of data we did not find any documentation of hemoglobinopathies although it is possible that they were never evaluated.

Anemia in the elderly has been shown to be associated with functional decline, poor cardiovascular outcomes and overall increased morbidity and mortality [7,12,18,20]. A number of studies have highlighted the association between anemia and impaired performance-based mobility function and even after adjustment for confounding factors like sex, age, body mass index, and other diseases, anemia was found to be significantly associated with a 1.91 times greater risk for recurrent falls [17,19]. Mortality risk during hospitalization and after discharge was also higher among the anemic elderly [18]. Because of the multifactorial nature of falls we could not correlate it with anemia on our study. Interestingly, the average BMI of more than 85% of study subjects was reasonable with no significant racial differences. We did not evaluate various causes for mortality in our study since a number of subjects died at home and it was difficult to clearly define the cause of death.

Anemia has also been found to be associated with impaired cognition in the elderly, in both medical and surgical settings [21,25,26]. A causative factor for delirium in acute care settings could be cardiac arrhythmias since fluctuating cardiac output could produce cerebral hypoxemia, inhibiting neurotransmitters in the brain [21-25]. We did not find any find any documentation of delirium in our review of the records which might reflect a lack of recognition of delirium by the providers or misidentification of delirium with dementia. However, the diagnosis of dementia was entered in the medical records and was noted to be higher in anemic subjects and more in African Americans (48%) vs White, Non-Hispanics (42%). Our findings support previous studies that have shown a two to three times higher prevalence of cognitive impairment among older African Americans compared to White, non-Hispanics [27]. It is plausible that there is an over-diagnosis of dementia in African Americans because cognitive evaluation and scores can be influenced by educational level, socioeconomic status, emotional outlook, communication and perspectives of both patients and providers [28].

In our study, chronic kidney disease was the most common co-morbid condition associated with anemia, being present in about a third of the subjects. Kidney failure leads to reduced erythropoietin production which not only produces anemia but has also been linked with neuro degeneration and the development of dementia [29-33]. In our study, the degree of kidney failure and its prevalence was similar between African Americans and White, Non-Hispanics. These findings differ from literature in which African Americans appear to be at a higher risk for developing chronic kidney disease versus Caucasians [32,33]. It is possible that our subset of nonagenarian and centenarian African Americans had a better molecular renal profile.

Iron deficiency was the second most common condition associated with anemia in our study population. Low levels of iron and vitamin B12 have both been associated with reduced brain oxygenation, development of dementia and even strokes [34,35]. Incidentally, B12 deficiency was also high on the list of potential contributing causes of anemia in our population. Iron deficiency and anemia have been associated with heart failure and a higher risk of death from any cause [36-39]. In an observational study of more than 4,000 patients attending a heart failure clinic, about 30% were found to be anemic, and the majority were iron deficient [36]. The incidence of heart failure in African Americans was reported to be 25% higher compared to Caucasians and this has been attributed to modifiable risk factors including elevated systolic blood pressure, coronary heart disease, and smoking [39-40]. Contrary to literature, our data indicated a slightly higher percentage of White, Non-Hispanic patients with a diagnosis of heart failure vs African Americans. However, in both racial groups the diagnosis of heart failure was more common in anemic vs non-anemic patients which is in accord with other studies reported in literature [36-40]. Interestingly, African American subjects in our study had significantly lower iron levels versus the White, Non-Hispanics. Considering that heart failure, dementia and strokes are age-associated diseases, both iron deficiency and anemia should be identified and treated appropriately in every older adult [34-40].

Disorders of the thyroid gland have been linked to anemia, and the underlying reasons range from impaired absorption of nutrients and autoimmune disease thyroid conditions, to differential expression of endocrine regulatory genes [41-43]. Studies suggest that Graves' disease appears to be more predominant in African American women compared to White, non-Hispanic women, whereas Hashimoto Thyroiditis incidence was highest in White, non-Hispanics and lowest in African Americans [43]. Our findings appear to be consistent with the reports of a higher prevalence of hypothyroidism in White, non-Hispanics versus African Americans elderly.

Mild anemia can produce vague signs and symptoms such as fatigue, weakness, shortness of breath and confusion which are often mistaken for a reduced functional capacity due to aging or some other disease [44]. In our study the overall degree of anemia was mild, which suggests resilient genes conferring health in these nonagenarian and centenarian individuals. There were also no significant racial differences except for a greater iron deficiency in African Americans which could have a potential nutritional, medication-related or a genetic basis [45]. The etiological reasons for racial differences in anemia will require further study. Meanwhile, we need to continue our efforts to reduce health disparity and provide better access to healthcare across all racial and socio-economic groups [46].

LIMITATIONS OF THE STUDY

The study suffers from the limitations of missing data common in retrospective analysis. In some instances, the only available data was from associated hospitalizations, which may have skewed the data towards a higher prevalence of anemia. We did not have sufficient information on nutritional status, lifestyle, or socioeconomic data, all of which could have contributed to hematological health. It is possible that specific diagnoses such as cancers were missed, or signs and symptoms were not investigated because of the advanced age of the patients, or per patient or caregivers' request. In addition, healthcare disparity and reduced access to care might have also contributed to misdiagnosis in some instances.

CONCLUSION

Anemia is common even in the oldest old. Overall, the very elderly in this study appeared to have "escaped" having clinically significant hematological malignancies or solid tumors. Although the prevalence of anemia was higher in African Americans with greater iron deficiency, in general their hematological profile was very similar to that of White, non-Hispanics. Since anemia is associated with significantly increased morbidity and mortality and is a treatable condition, timely evaluation and management is warranted to reduce the healthcare burden and improve the quality of life. Finally, more studies are needed to elucidate the molecular mechanisms responsible for maintaining hematological health with advancing age.

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Conflicts of Interest

The authors declare that there is no conflict of interest regarding the publication of this paper.

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