

ORIGINAL RESEARCH

Medicine Science 2018;7(4):919-22

Prevalence of anemia types and etiology in patients with anemia

Mehmet Zahid Kocak, Gulali Aktas, Edip Erkus, Tuba Duman, Burcin Atak

Bolu Abant Izzet Baysal University, Faculty of Medicine Department of Internal Medicine, Bolu, Turkey

Received 14 July 2018; Accepted 01 August 2018

Available online 18.10.2018 with doi:10.5455/medscience.2018.07.8911

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Abstract

In this study, we aimed to determine the frequency and etiologic causes of anemia types in a university clinic who were diagnosed with anemia, whether there were differences in anemia types by gender difference, and the relation of anemia types according to age and comorbidity. A total of 250 patients were included in the study. Iron deficiency anemia alone in 151, B12 deficiency anemia alone in 18, folate deficiency anemia alone in 2, anemia of chronic diseases in 11 and mixed anemia in 65 cases were detected. Underlying etiology of the anemia cases were diagnosed in 173 (69%) of the patients, however, the etiology of the anemia remained unclear in 77 (31%) cases. Iron deficiency was more frequent in women than in men ($p < 0.001$). Mixed anemia was detected in 65 patients. Of these, 41 (64%) had both iron deficiency and B12 deficiency anemia; 12 (18%) had both iron deficiency and folic acid deficiency; 4 (6%) had both B12 and folic acid deficiency; and 8 (12%) had iron, B12 and folic acid deficiencies. The most common type of anemia is iron deficiency anemia and is more prevalent in women. However, the frequency of other types of anemia is too high to be underestimated. Informing the patients about the anemia and its complications can make these patients more willing to proceed with further examination and thus, early diagnosis and treatment can reduce morbidity and mortality.

Keywords: Anemia frequency, anemia classification, etiology, iron deficiency, B12 deficiency, mixed anemia

Introduction

Anemia develops as a result of various causes and is defined as a decrease in erythrocyte count or hemoglobin (Hb) concentration. Anemia is not a disease, it is a finding and it is necessary to find out what the underlying cause is. Many etiologic factors cause anemia and many anemia types are defined according to the underlying cause. Globally, it is reported that iron deficiency is the most important factor affecting the development of the anemia [1]. It is generally assumed that 50% of anemia cases are due to iron deficiency [2], but this rate may vary between populations, and in many international studies, the prevalence of anemia has been shown to vary from population to population [3-5].

According to the Third National Health and Nutrition Examination Survey (NHANES III), anemia is roughly divided into three subtypes: anemia with nutrient deficiencies such as iron, folate or vitamin B12 deficiencies; anemia without nutrient deficiencies such as renal anemia or chronic anemia; and anemia which cannot be classified and thus called “unexplained anemia” [3]. In this

study, the frequency of these anemia subtypes were reported to be similar [3]. In some studies, it has been shown that anemia of chronic disease was the most common subtype in elderly [6,7].

In this study, we aimed to determine the frequency and etiologic causes of anemia types in subjects presented to a university clinic, whether there were differences in anemia types by gender difference, and the relation of anemia types according to age and comorbidity.

Materials and Methods

In this study, 250 patients who were admitted to Abant Izzet Baysal University Medical Faculty, Internal Medicine outpatient clinics between October 2015 and 2017 for various reasons and who were found to have anemia as a result of the examinations and laboratory studies were retrospectively evaluated. The study was initiated after receiving the necessary authorization from the institutional board. Patient information was obtained from the outpatient clinic registry system. Patients older than 18 years of age and Hb < 12 mg / dL in women with Hb and < 13 mg / dL in men were included to the study. Mean corpuscular hemoglobin concentration, mean corpuscular hemoglobin, iron, total iron binding capacity, ferritin, B12 and folic acid, Hb, hematocrit (Htc), mean corpuscular volume (MCV), erythrocyte count, erythrocyte

*Corresponding Author: Mehmet Zahid Kocak, Bolu Abant Izzet Baysal University, Faculty of Medicine Department of Internal medicine, Bolu, Turkey
E-mail: mehmetzahidkocak@hotmail.com

distribution width and routine biochemical values were recorded. Transferrin saturation (%) was calculated by using iron and total iron binding capacity values. Lower levels from 25 µg / dl for serum iron, 15 ng / ml for ferritin, 4 ng / ml for folate and 203 pg / ml for vitamin B12 were considered as deficiency [8]. History of gastric resection, age, sex, history of previous surgery, drug usage, gastrointestinal bleeding history, pica, hemorrhoids, history of colon tumor were observed from medical data. Comorbidities of study population were recorded. The underlying causes of patients diagnosed with anemia etiology were noted. Patients who were not identified with anemia etiology were also recorded separately.

Statistical analysis

The collected data were recorded on a statistics software (SPSS 15.0 for Windows, IBM, Chicago, IL, USA). Kolmogorov-Smirnov test was used to assess whether the variables fit the normal distribution. In the analysis of normal distribution variables, t test was used and values were expressed as mean ± standard deviation. Mann-Whitney U test was used for the analysis of the variables without normal distribution and the values were expressed as median (minimum-maximum). Chi-square test was used for comparison of categorical variables between study groups. $P < 0.05$ was determined as statistical significance level.

Results

A total of 250 patients 37 male (15%) and 213 female (85%) were included in the study. The incidence of anemia in women was higher than in men ($p < 0.001$). The mean age of men was 56.14 ± 19.9 , while the mean age of women was 38.23 ± 16.6 . Women were significantly younger than men ($p < 0.001$). The Hb level of the women was 10.5 (6.06-11.9) mg / dL and the Hb level of the men was 10.8 (5.8-11.9) mg / dL ($p = 0.04$). 193 (90.6%) of the women were younger than 65 years old while 20 were older than 65 years of age. While 23 (62.2%) of the males were younger than 65 years, 14 (37.8%) were over 65 years old. The Hb value of patients aged > 65 years was 10.6 mg / dL in the study population, while the Hb level was > 10.35 mg / dL in those > 65 years ($p = 0.63$). The number of anemic patients in the geriatric age group was lower in both sexes, but there was no significant difference between the Hb values of the geriatric age group and the younger patients.

When evaluated in terms of anemia type, 151 patients (134 women and 17 men) had isolated iron deficiency anemia. Iron deficiency anemia was more frequent in women than in men ($p < 0.001$). In our study, there were 18 patients with vitamin B12 deficiency anemia alone and 8 (44%) of them were women and 10 (55%) were men. There was no significant difference between the sexes in terms of vitamin B12 deficiency anemia frequency ($p = 0.06$). Only two patients had folic acid deficiency anemia alone. Both of these patients were women. There were 14 patients with anemia of chronic disease alone; 11 of them (78%) were female and 3 (22%) were male and there was no statistically significant difference between the sexes ($p = 0.343$). Mixed anemia was detected in a total of 65 patients. Iron deficiency and B12 deficiency anemia together seen in 41 (39 women and 2 men), iron deficiency and folate deficiency together seen in 12 (10 females, 2 males), B12 and folate deficiency anemia together seen in 4 (1 woman and 3 men) and iron, folate and B12 deficiency anemia together seen in 8 (all were women) patients. Mean MCV of patients with mixed

anemia was 78.57 ± 1.27 fL.

Of the 151 patients with iron deficiency anemia alone, 21 (14%) had comorbidities such as hypertension, type 2 diabetes mellitus, chronic gastritis, coronary artery disease. The anemia was accompanied by concomitant diseases in 16 (88%) of 18 patients with B12 deficiency alone and in 13 (20%) of 65 patients with mixed anemia. The age of the anemic patients with comorbidities was 52 (21-90), while the age of subjects without comorbidities was 36 (19-88) ($p < 0.001$). The Hb value of the patients with and without comorbidities were 10.6 (5.83-11.9) mg / dL and 10.5 (5.86-11.8) mg / dL, respectively ($p = 0.78$).

Underlying causes of the iron deficiency anemia were menometrorrhagia in 82 (54.3%), bleeding due to hemorrhoid in 19 (12.6%), nutritional insufficiency in 7, malignancy in 2 of the cases. Underlying cause of the anemia could not be detected in 41 of 151 patients with iron deficiency anemia alone. The underlying causes of B12 deficiency anemia were chronic atrophic gastritis in 11 (61.1%) and inadequate nutrition in 7 (38.9%) of the cases. The etiological cause of 2 patients with folic acid deficiency could not be established. Causes of mixed anemia were pregnancy in 3 (4%), menorrhagia or gastrointestinal blood loss in 27 (43%), nutritional deficits in 15 (23%) of the case. In 20 (30%) cases with mixed anemia, underlying cause or causes could not be determined. Eight of the 14 patients (50%) with anemia of chronic disease were due to chronic kidney disease and 6 were (50%) due to malignant diseases. When all of the study populations were evaluated, underlying causes of the anemia were detected in 173 (69%) of the cases 77 (31%) cases remained as unclear etiology. The age of the patients with clear underlying cause (36 ± 16.1 years) were significantly younger than the patients with unclear underlying cause (51.3 ± 18.6 years) ($p < 0.001$). It has been found that the etiology of anemia is easier to detect in younger patients. The etiology of anemia could not be determined in 27% of women (57 of 213 women) and 54% of men (20 of 37). The difference between the sexes was statistically significant ($p = 0.001$).

The mean hemoglobin of the patients was 10.18 ± 1.25 g / dL, the mean hematocrit was $32.11 \pm 3.69\%$ and the mean MCV was 80.31 ± 43 fL. Patients with iron deficiency anemia had ferritin 8.1 mg / dL (1.72-4.78), iron 18,57 µg / dL (17-20.14), total iron binding capacity 422 (413-431), transferrin saturation 3.8% (1-18). Vitamin B12 levels were 153.89 pg / ml (83-192) in those with B12 deficiency anemia, while folic acid level in the folic acid deficiency patients was 2.4ng / ml (2.3-2.5). The transferrin saturation of the cases with combined anemia was 3.9% (2-21%) while this value was found to be 24.1% (2-387%) in the cases with anemia of chronic disease.

Discussion

The most important consequences of this study are that the most common type of anemia in patients admitted to a tertiary health center is the anemia of iron deficiency and the majority of patients are women. Anemic women were younger than anemic men. However, Hb levels were not statistically different between men and women. The number of geriatric anemic subjects was found to be lower than in younger patients, but no difference was found in terms of Hb values. In our study, the underlying cause of anemia could not be determined in almost one third of the patients (77 of

250 patients).

In a study conducted in anemic patients, 73% of the patients had anemia due to iron deficiency, 2.7% had drug associated anemia, and 18.9% had no detectable cause of the anemia [9]. Iron, folate, B12 and vitamin A levels were investigated in anemic pregnant women and 23% of the cases had iron deficiency alone, 32% of the cases had iron deficiency in addition to at least one of folate, vitamin B12 and vitamin A deficiencies, 26% at least one of folate, B12 and vitamin A deficiency that not accompanied by iron deficiency, 19% had no deficiency in iron, folate, B12 or vitamin A levels [10]. Another study in 190 geriatric subjects with anemia showed that the rate of anemia due to iron deficiency was 12%, the rate of unexplained anemia was 35%, and the rate of possible myelodysplastic syndrome was 16% [11]. Authors suggested that approximately one third of the anemia in elderly individuals was caused by deficient iron, folate or B12 vitamins, and one third caused by chronic renal disease or other chronic conditions, and the remaining one third categorized as unclassified or unexplained anemia [3]. The most common cause of anemia in our study was iron deficiency. This finding is similar to the literature knowledge. Other causes of anemia in present study were B12 deficiency, anemia of chronic disease and folic acid deficiency. 31% of subjects in our study had no detectable cause of underlying etiology that was similar to the literature findings. It is noteworthy that these unclear anemia cases have not had the necessary tests for diagnosis.

According to the World Health Organization survey, the prevalence of anemia was 69% in pregnant women and 73.5% in non-pregnant women, 40.2% in men and 39.1% in the elderly [2]. The prevalence of anemia in fast-developing countries was estimated at 9%, while the prevalence in slow developing countries was 43% [12,13]. The most common cause of anemia is iron deficiency, which is more common in women than men [2]. The most common type of anemia in our study was also iron deficiency. Mixed anemia was the second most common type of anemia, and the most common component of these combined anemia was iron deficiency.

Low iron intake, poor absorption of iron due to phytate or phenolic compounds, iron loss from gastrointestinal or genitourinary system and increased iron requirement as seen in growth age children and pregnancy are the main risk factors for iron deficiency anemia. In present study, low iron intake and especially iron loss due to menorrhagia were noted as common causes of iron deficiency. Iron deficiency anemia is more frequent in women than in men [2,14]. In our study in accordance with the literature, the number of women who had iron deficiency anemia was higher than men.

Vitamin B12 deficiency has been reported to affect 10-15% of people over age 60 [15]. In the A prevalence of 12% among the elderly was reported in Framingham study [16]. Some other studies reported the prevalence of B12 deficiency as high as 30-40% in the elderly [17,18]. The absorption of vitamin B12 does not decrease with age. However, compared with the young population, the absorption of vitamin B12 is reduced in the geriatric age group due to high prevalence of atrophic gastritis [15]. In our study, 14 of the subjects with B12 deficiency anemia were younger than 65 years and only 4 were over 65 years of age. This inconsistency of our results and literature knowledge was due to the fact that low number of elderly patients in present study. Eight (44%) of

the patients with B12 deficiency were women and 10 (56%) were men. Atrophic gastritis was the most common underlying cause of B12 deficiency. Tight vegetarianism, which cause inadequate vitamin intake, was less common among etiologic factors for B12 insufficiency. No underlying causes were detected in 2 cases with folic acid deficiency in present report.

In our study, 200 patients had no additional disease while 50 had a chronic disease such as hypertension, diabetes mellitus and chronic kidney disease. The average age of those with comorbidities was higher than those without comorbidities. However, there was no statistically significant difference between Hb and Hct values according to the comorbidity. Although lower levels Hb expected in subjects with comorbidities, we could not showed such a result possibly due to the low number of subjects with chronic conditions in present study.

Conclusion

In conclusion, the most common type of anemia encountered by physicians in tertiary care is iron deficiency anemia. As advancing patient age, the likelihood of detecting the cause of anemia decreases. Most anemic patients with unknown cause are in the elderly population and these patients are those who do not want to have further examinations such as upper and lower gastrointestinal endoscopy. Informing the patients about the anemia and its complications can make these patients more willing to proceed with further examination and thus, early diagnosis and treatment can reduce morbidity and mortality.

Competing interests

The authors declare that they have no competing interest

Financial Disclosure

The financial support for this study was provided by the investigators themselves.

Ethical approval

Before the study, permissions were obtained from local ethical committee.

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