Evaluation of anemia frequency and etiologies in hospitalized patients in a tertiary pediatrics clinic

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ABSTRACT

Objective: Anemia, which is a public health problem on a global scale, continues to maintain its importance in pediatric patients. There are few studies on the prevalence of anemia in hospitalized children. This study was conducted to evaluate the prevalence and etiologies of anemia in hospitalized pediatric patients.

Material and Method: This is a cross-sectional epidemiological study. The study group consists of 1000 patients between the ages of 6 months and 18 years who were hospitalized in the Department of Pediatrics of Prof. Dr. Cemil Tascioglu City Hospital. The data of the patients were reviewed retrospectively. The SPSS 22.0 program was used for statistical analyzes and calculations and p< 0.05 was accepted for significance.

Results: Of the patients included in the study, 569 (56.9%) were male, and 431 (43.1%) were female. In the study, the number of patients with anemia was 276 (27.6%), and among those 151 (26.5%) were male and 125 (29.0%) were female. The highest rate of anemia in different age groups was in infancy, with 32.3%.

The number of patients with iron deficiency anemia was 121 (43.8%), anemia of chronic disease was 42 (15.2%), anemia of acute inflammation was 41 (14.9%), and anemia due to B12 deficiency was 31 (11.2%). It was determined that patients with anemia had a longer hospital stay than those without anemia. Moreover, the hospitalization period of patients with anemia of chronic disease was longer than those with iron deficiency anemia.

Conclusion: Anemia is an important problem in hospitalized children as well as in the general population. Iron deficiency is the most common etiology of anemia in hospitalized patients in the pediatric clinic similar to the general population. The hospitalization period was found to be significantly longer in anemic patients than in non-anemic patients. During hospitalization, children should be monitored for anemia and this duration of stay should be regarded as an opportunity to combat anemia or to provide necessary micronutrient or nutritional support to socioeconomically disadvantaged groups.

Keywords: Anemia, iron deficiency, pediatrics, hospital

INTRODUCTION

Anemia, which is considered a public health problem on a global scale, is defined as a decrease in hemoglobin or hematocrit levels below two standard deviations according to age, race, and gender (1-3). Worldwide, it is estimated that approximately one-quarter of the world's population has anemia, and this prevalence is higher in developing countries. Although anemia is common, the prevalence of anemia may vary according to the development level of countries. The anemia prevalence was reported as 9.1%, 25.7%, and 42.8% in high, middle, and low-income countries, respectively. The 2015 WHO report, derived from the global prevalence of anemia in 2011, showed that the highest frequency (42.6%) was in children compared to other age groups in the world (4). Despite a decline in prevalence globally, total cases of anemia rose from 1.42 billion in 1990 to 1.74 billion in 2019. The greatest burden of anemia was found in west and central sub-Saharan Africa and South Asia, while the highest prevalence of combined anemia (39.7%) was found in children under the age of five (5). When the anemia causes are examined according to etiologies, iron deficiency anemia is the leading one. It is estimated that around 50% of anemia cases are attributed to this micronutrient deficiency, however, this rate likely

varies considerably between regions and countries. Other causes of anemia include other micronutrient deficiencies such as folic acid and vitamin B12 deficiencies; the presence of infectious diseases and genetic hemoglobin disorders (6, 7).

In epidemiological studies, it was found that anemia is associated with impaired neurocognitive outcomes, including learning difficulties, corrupted memory and processing speed, and emotional instability. Iron, folic acid, and vitamin B12 are essential for brain development and function. In general, a deficiency of these micronutrients results in decreased myelin production by altering gene and protein profiles, which can regulate central nervous system development processes. Impaired synaptogenesis and neural repair may lead to delays in brain development or dysfunction (8-11).

There are different anemia rates among hospitalized children in line with the sociocultural level and developmental state of countries. The presence of anemia augments the treatment process and the risk of hospital stay (4). Our aim in this study is to evaluate our hospitalized patients in terms of the prevalence of anemia and to discuss possible complications of this condition with the precautions that can be taken in this regard.

MATERIAL and METHODS

This study was performed on 1000 children between the ages of 6 months and 18 years who were hospitalized in the Department of Pediatrics of Prof. Dr. Cemil Tascioglu City Hospital between 01.03.2019 and 01.03.2020 and meet the inclusion criteria of the study. The patients with missing data were excluded from the study. This study is a cross-sectional, retrospective epidemiological study. Patients younger than six months and older than 18 years of age, and patients hospitalized in neonatal intensive care, pediatric intensive care, and/or pediatric hematology wards were not included in the study. The patients were divided into three groups according to their ages; those aged 6-24 months were included in the infancy period, those aged 3-9 years were included in the childhood period, and those aged 10 -18 years were included in the adolescence period (12). Demographic characteristics of the patients, diagnosis of hospitalization, duration of hospitalization, presence of anemia, transfusion information, presence of chronic diseases, complete blood count parameters at admission and discharge, ferritin, vitamin B12, foliate, C-reactive protein levels were recorded from the patient files. Anemia was diagnosed based on the reference values (13). This study was carried out in accordance with the Helsinki declaration, after the approval of the clinical research ethics committee of Cemil Tascioglu City Hospital (the date 26/01/2021 and number 26).

Statistical Package for the Social Sciences (SPSS) program was performed to evaluate and analyze the research data. Numerical data were reported as mean (standard deviation) and median (minimum-maximum); while the categorical data were given as numbers and percentages. Kolmogorov-Smirnov and Shapiro-Wilk tests were used to determine the conformity of the data to the normal distribution. Parametric tests were performed if the data met the necessary assumptions, and non-parametric tests were used if they did not. The statistical significance was set at $p < 0.05$.

RESULTS

In the study, which was carried out to determine the frequency and the etiology of anemia in hospitalized children, 1000 patients (569 boys and 431 girls) were examined and their demographic characteristics are summarized in Table 1.

While anemia was not detected in 724 (72.4%) of 1000 patients included in the study; anemia was present in 276 (27.6%) patients. Accordingly, the prevalence of anemia was found to be 27.6% in patients hospitalized in our clinic. The prevalence of anemia was found to be 26.5% in boys and 29.0% in girls.

The rate of anemia was 54.7% male and 45.3% female. According to the analysis for the etiology of anemia by gender, 63.6% of patients with iron deficiency, 52.4% of patients with anemia of chronic disease, 51.2% of patients with anemia of acute inflammation, and 43.1% of patients with other etiologies were male and there was a statistically significant difference between the genders regarding the etiology of the anemia (Table 2).

Of 276 patients with anemia, 121 (43.8%) were having iron deficiency anemia, 42 (15.2%) were having anemia of chronic diseases, 41 (14.9%) were having anemia of acute inflammation, and 31 (6.9%) were having B12 deficiency anemia (Table 3).

In addition to being the most common cause of all anemia cases, iron deficiency anemia is the leading cause of anemia with 50.3% in infancy, 23.1% in childhood, and 32.5% in adolescence.

As summarized in Table 4, 849 (84.9%) of the patients did not have a chronic/concomitant disease, while a concomitant chronic disease was detected in 151 (15.1%) of the patients. Among these diseases, epilepsy was the most common with a 24.5% prevalence.

According to the analysis performed to compare the length of stay in the hospital according to the etiology of anemia, the average length of stay (minimum-maximum) of patients diagnosed with iron deficiency was 3 (2-23) days; it was 6 (2-21) days in patients with anemia of chronic disease, 4 (1-25) days in patients with anemia due to acute infection, 4 (2-15) days for anemia due to B12 deficiency, and 4 (2-23) days for other etiologies of anemia.

There was a statistically significant difference between the groups regarding the hospitalization periods ($p < 0.001$). When anemia of chronic disease was compared with iron deficiency, a statistically significant difference was found, prolonging the length of hospital stay. No statistically significant difference was found in the pair-wise comparisons of the other groups (figure 1).

As seen in Figure 2, when the duration of hospitalization is compared according to the presence of anemia, the average length of stay in the hospital for patients with anemia (minimum-maximum) was 4 (1-25) days, and the average duration of hospitalization for patients without anemia (minimum-maximum) was 3 (1- 14) days and there was a significant difference between the groups ($p < 0.001$).

When the etiologies of anemia were compared according to the erythrocyte suspension transfusion requirements, the highest transfusion requirement was observed in patients with anemia of chronic disease with a rate of 23.8%.

As seen in Table 5, the difference between the groups was statistically significant (p=0.003).

Of the patients included in the study, 384 (38.4%) were in infancy, 451 (45.1%) were in childhood, and 165 (16.5%) were in adolescence. The prevalence of anemia in infancy was 32.3%, it was 24.8% in adolescence, and 24.6% in childhood. According to the analysis performed to compare the presence of anemia by age groups, there was a statistically significant difference between the groups. According to the pair-wise comparisons of the groups, the difference between infancy and childhood was statistically significant in that anemia was more common in infancy. However, the difference between infancy and adolescence and between childhood and adolescence was not statistically significant.

According to the analysis performed to compare the hospitalization and discharge hemoglobin levels of the patients (patients with erythrocyte suspension were not included in the analysis, n=307) the mean (± standard deviation) admission hemoglobin level was 11.71 (±1.63) g/dl and discharge hemoglobin (standard deviation) was 11.50 (±1.54) g/dl, and a statistically significant difference was found between the two groups (p<0.001). Accordingly, the hemoglobin measurement of the patients at discharge was 0.21 g/dl lower than the hemoglobin level at admission. The mean (±standard deviation) hospitalization hemoglobin of the patients in infancy was 10.98 (±1.30) and the mean discharge hemoglobin was 10.70 (±1.25) g/dl, and the difference was statistically significant. The mean (±standard deviation) hospitalization hemoglobin of the adolescent patients was 12.92 (±1.96) and the mean (±standard deviation) discharge hemoglobin was 12.69 (±1.88) g/dl, and the difference was found to be statistically significant (p<0.001).

Table 1. Demographic features of the study participants

Feature	Number (n)	Percentage (%)
Gender		
Male	569	56.9
Female	431	43.1
Age groups		
Infancy period (6 months-2 ages)	384	38.4
Childhood period (3-9 years)	451	45.1
Adolescence period (10-18 years)	165	16.5
Total	**1000**	**100**

Table 2. Comparison of the etiology of the anemia between genders

	Gender			
Etiology	Male n (%)	Female n (%)	Total n (%)	p
Iron deficiency	77 (63.6)	44 (36.4)	121 (100.0)	
Chronic diseases	22 (52.4)	20 (47.6)	42 (100.0)	
Acute infections	21 (51.2)	20 (48.8)	41 (100.0)	0.043
Others	31 (43.1)	41 (56.9)	72 (100.0)	
Total	151 (54,7)	125(45,3)	276 (100)	

Table 3. Anemia frequency and etiology

Anemia etiology	Number(n)	Percentage(%)
Iron deficiency anemia	121	43.8
Anemia of chronic diseases	42	15.2
Anemia of acute inflammation	41	14.9
B12 deficiency anemia	31	11.2
Iron and B12 deficiency anemia	14	5.1
Chronic diseases and iron deficiency anemia	5	1.8
Foliate, B12, and iron deficiency	5	1.8
Idiopathic	3	1.1
Anemia due to acute hemorrhage	3	1.1
Foliate deficiency	3	1.1
Thalassemia Intermedia	3	1.1
Sickle cell anemia	2	0.7
Thalassemia Major	2	0.7
Hereditary Spherocytosis	1	0.4
Total	**276**	**100.0**

Table 4. Chronic/concomitant disease

Feature	Number (n)	Percentage (%)
Concomitant disease		
Present	849	84.9
Absent	151	15.1
Total	**1000**	**100.0**
Disease		
Epilepsy	37	24.5
Frequent asthma or bronchitis attacks	20	13.2
Congenital cardiac disease	16	10.6
Down Syndrome	11	7.3
Cerebral Palsy	9	6.0
Inflammatory bowel disease	9	6.0
Hypothyroidism	8	5.3
Malignity	8	5.3
Celiac disease	7	4.6
Tuberculosis	5	3.3
Nephrotic Syndrome	5	3.3
Autism Spectrum Disorder	5	3.3
Chronic Liver diseases	5	3.3
Factor 8 Deficiency	4	2.6
Others	2	1.3
Total	**151**	**100.0**
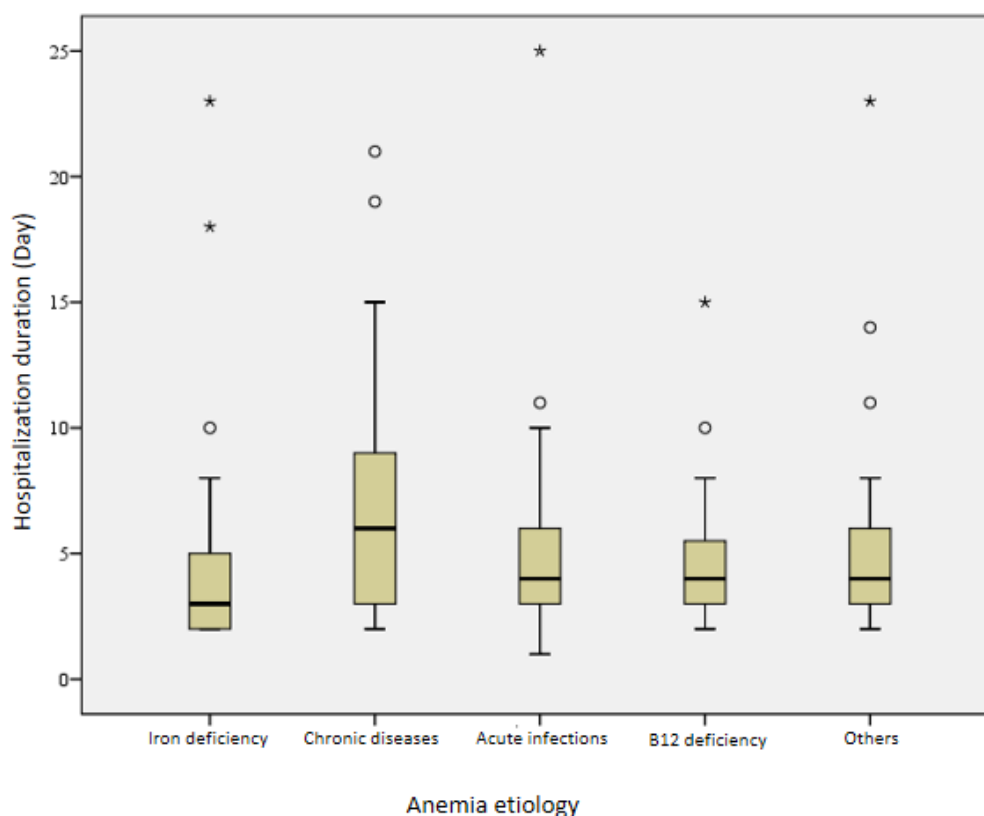
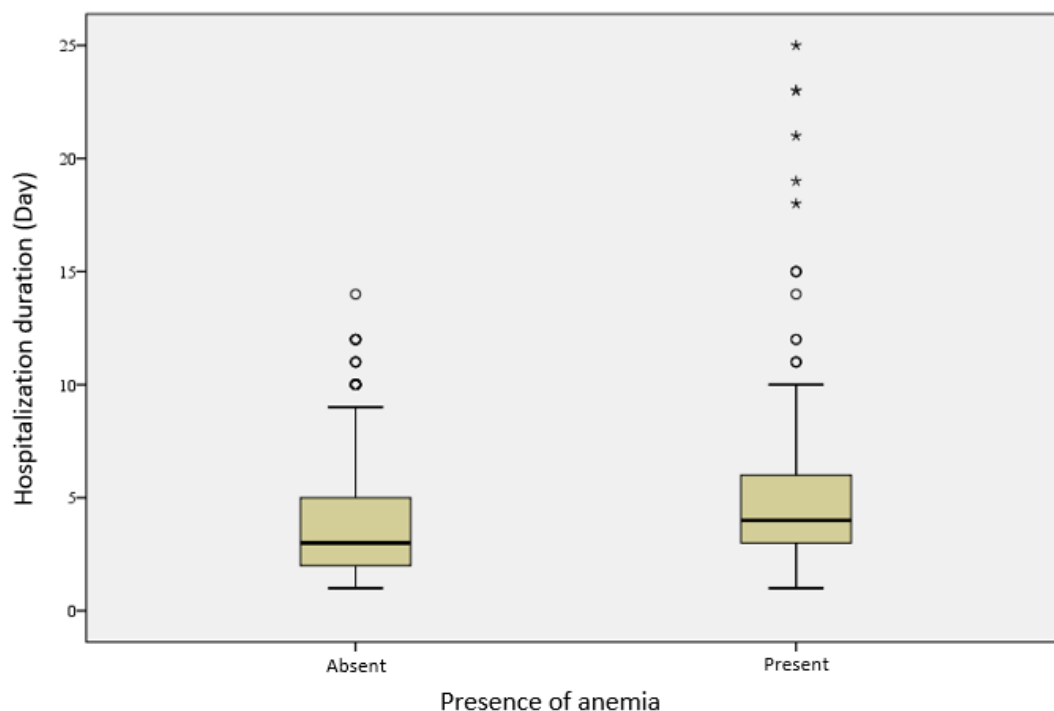**Figure 1.** Duration of hospitalization regarding the anemia etiology

Figure 2. Hospitalization duration in the presence of anemia

Table 5. Comparison of erythrocyte suspension transfusion requirements according to the etiology of anemia

	Erythrocyte suspension requirements			
Etiology	Absent n (%)	Present n (%)	Total n (%)	p
Iron deficiency	115(95.0)	6(5.0)	121(100.0)	
Chronic diseases	32(76.2)	10(23.8)	42(100.0)	0.003
Acute infections	38(92.7)	3(7.3)	41(100.0)	
Others	66(91.7)	6(8.3)	72(100.0)	

DISCUSSION

The general prevalence of anemia in the world is around 42.6%. In our study, the prevalence of anemia was found to be 27.6%. Salami et al. (15) found the prevalence to be 33.2% in a study conducted in hospitalized pediatric patients aged between 1 month and 12 years. The prevalence of anemia was found to be 62.3% in a study conducted on the African continent, (4). In Europe and similarly developed countries, the prevalence of anemia was around 15% which is lower (16). The prevalence of anemia in the world is in a wide range according to age groups and socio-cultural levels. Although the rate we found in our study included hospitalized patients, it is compatible with the general population values of the literature. The decrease in anemia in proportion to the level of development shows that access to micronutrients and other nutrients is a fundamental factor. As a matter of fact, in the study of Salami et al.(15), children with malnutrition encountered anemia 3.4 times more than those without malnutrition.

Anemia in childhood is most common between the ages of 6 months and 2 years (17). The higher prevalence of anemia in infants is mostly attributed to the inability to meet the increasing need proportional to the increasing growth rate (18). In our study, the prevalence of anemia in infancy was found to be 32.3% and higher than that of other age groups, in line with the literature.

Zuffo et al. (19) found the prevalence of anemia in children younger than 24 months to be 39.9%. This rate was higher than other age groups, similar to our study. Sayar et al. (20) found the prevalence of anemia in the neonatal period to be 3.2% in their study conducted with healthy newborns and infants, while they found this rate to be 22.3% in the 6th-month control of the same children. As can be understood from the literature, we can say that this period is important in terms of micronutrient support.

Secondly, the highest frequency of anemia is seen in the adolescent age group (17). In our study, this rate was 24.8%, and it was the period in which anemia was seen with the second frequency. In the study of Dugdale et al., this frequency was found to be 27% in developing countries and 6% in developed countries (21). In a study conducted in our country, this frequency was found to be 12.5% (22). The lower prevalence in our study may be due to the selection of our patient group from hospitalized patients. It can be thought that anemia is more common in this age group, which may be due to the increased muscle strength and growth in boys, and growth and menstruation in girls.

When all age groups were included in our study, 54.7% of the patients diagnosed with anemia were male. Similarly, Enawgaw et al. (4) found that 55.2% of the patients with anemia were male.

This can be explained by the fact that anemia is more common in boys compared to girls due to rapid development in the pre-school period (23). On the other hand, in a study conducted by Salami et al.(15) in which they evaluated hospitalized patients, although anemia was more common in males, they could not find a statistical difference. Some studies are the opposite of this and found anemia more commonly in females (24, 25).

When patients with anemia were examined, the most common etiological factor was iron deficiency anemia with 43.8%. In a study conducted by Çetinkaya et al. in hospitalized patients, they found the prevalence of iron deficiency anemia to be 61.6% (26). In a prevalence study conducted by Balci et al. in adolescent patients, they found the rate of anemia to be 5.6%. Among all anemia, iron deficiency anemia was the most common (24). In the study of Silva et al., they found the prevalence of iron deficiency anemia to be 10.3%, but in the same study, the rate of iron deficiency was found to be 37.4%. In a study conducted on hospitalized children from Turkey, the frequency of iron deficiency anemia was found to be 16.5% (27). As can be seen, studies are reporting different frequencies. Iron is a very important micronutrient, especially in childhood age groups. Its deficiency causes iron deficiency and iron-deficiency anemia. After understanding the importance of this condition, countries started to give iron supplements in certain age groups as a part of preventive health services. As a matter of fact, as a part of this struggle since 2004, prophylactic iron supplementation has been applied to all infants from 4 months of age with the "Turkey as iron" campaign in our country. This treatment is applied free of charge until the age of 1 (28). Although positive results have been obtained with this treatment, unfortunately, we are still far from the target of reducing it to 5% and below recommended by the World Health Organization. More education and nutritional support should be provided to socio-culturally disadvantaged groups. However, patients who do not receive prophylaxis should be checked for anemia with certain follow-up programs. There are follow-up guidelines published for these controls in our country (29).

B12 deficiency anemia is another common nutritional anemia in developing countries, and it has been reported that it is more common especially in children and pregnant women (30). In studies conducted in regions with low socioeconomic status, the frequency of B12 deficiency has been reported to vary between 22-65% (31). Naiboglu et al. (27) found the frequency of B12 deficiency to be 51.5% in their study on children hospitalized due to lower respiratory tract infection. In our study group, the rate of patients with B12 deficiency anemia was found to be 11.2%. When combinations of B12 deficiency with other etiologies are included, B12 deficiency anemia constitutes 18.1% of all anemia cases. B12 deficiency continues to be important in developing countries, especially due to nutritional deficiencies.

In our study, when the relationship between anemia and the length of stay of the patients was examined, a significant relationship was found, and the hospitalization period of patients with anemia was higher than those without anemia. Salami et al (15) did not find any significant relationship between anemia and hospitalization periods. However, it is not easy to explain the hospitalization period only with anemia. It is obvious that this may change depending on the

underlying disease and treatment processes. On the other hand, a significant correlation was found between the etiology of anemia and the need for transfusion of erythrocyte suspension during their hospitalization, and the group with the most frequent transfusion requirement was the patients with anemia of chronic disease. These patients may have had higher transfusion needs than non-hospitalized patients with iron deficiency due to their other accompanying health problems. The discharge hemoglobin levels of our patients who were not transfused were found to be lower than the hospitalization hemoglobin levels. Since our hospital is a tertiary center, we think that this situation occurs due to the hospitalization of patients who require more examinations and investigations.

Our study has some limitations. Since our study was retrospective, it was not possible to reach the socioeconomic data of our patient group, the information about whether the patients received iron prophylaxis, their dietary habits, and histories from the file information.

CONCLUSION

In conclusion, this study showed that anemia is an important problem in hospitalized children, iron deficiency anemia is the most common etiological cause in this group, as in the general population, and that the hospitalization period in anemic patients is longer than that of the non-anemic patients. During hospitalization, as in public health monitoring programs, children should be monitored for anemia and hospitalization should be seen as an opportunity to combat anemia or to provide necessary micronutrient or nutritional support to socioeconomically disadvantaged groups.

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