Rom J Morphol Embryol 2023, 64(3):419–426 ISSN (print) 1220–0522, ISSN (online) 2066–8279 doi: 10.47162/RJME.64.3.13

ORIGINAL PAPER

RJME Romanian Journal of Morphology & Embryology http://www.rjme.ro/

Associated factors in pediatric patients admitted with severe iron-deficiency anemia in the last seven years – the experience of a single pediatric unit

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Abstract

Objectives: To study the causes of iron deficiency, laboratory findings and clinical manifestation of infants aged 6–12 months and children aged 1–3 years diagnosed with severe iron-deficiency anemia. *Patients, Materials and Methods*: We conducted an observational, retrospective single tertiary center study between January 2015 and April 2022, which included 142 children. The control group (patients with no diagnosis of severe iron-deficiency anemia) included 71 patients and the study group (patients diagnosed with severe iron-deficiency anemia) included also 71 patients. Clinical data were retrospectively collected from hospital medical records. Statistical analysis was conducted using Statistical Package for the Social Sciences (SPSS) 25.0 software. *Results*: Seventy-one children had hemoglobin <7 g/dL and low values of ferritin/serum iron (22 infants aged 6–12 months and 49 children aged 1–3 years). In both the study and control groups, the male gender was slightly more prevalent. Mother's age at birth and living standard is significantly lower in the study group. We note a higher frequency of premature births (14.08%) in children identified with anemia compared to control group (8.45%). We found a statistically significant distribution of cow's milk consumption among the two groups (p<0.001). Pearson's correlation test revealed a significant positive correlation, indicating that anemia is directly proportional to cow's milk consumption. *Conclusions*: The most frequent cause of iron-deficiency anemia in infants and children 1–3 years old was the consumption of cow's milk following incorrect diversification and incomplete prophylaxis of iron-deficiency anemia.

Keywords: severe iron deficiency, anemia, infants, children, cow's milk.

Introduction

Iron-deficiency anemia is a disorder of hemoglobin (Hb) synthesis resulting from a decrease in the body's overall iron stores, biologically expressed as hypochromic, microcytic anemia. Iron deficiency is the most common and severe nutritional deficiency affecting disadvantaged socio-economic groups worldwide [1]. Young children aged six months to three years are at higher risk of iron-deficiency anemia due to increased dietary iron needs and limited access to iron-containing foods [2–4]. The *World Health Organization* (WHO) has recognized that the incidence of iron-deficiency anemia in children less than five years old may be less than 50%. The *WHO* estimated that 44% and 65% of children with iron-deficiency anemia in the European region had a favorable response to iron supplementation [5]. The prevalence of iron-deficiency anemia in children under the age of 5 has recently been estimated between 1% and 4% in the UK, the USA, and other developed countries. The incidence of iron-deficiency anemia in children is higher, as described in the literature in regions such as Africa, South Asia, and Latin America, with a prevalence between 45% and 65% [6]. Severe iron-deficiency anemia (hypochromic, microcytic, Hb <7 g/dL, low serum iron level, and serum ferritin) is a major condition justifying hospitalization. These children present lethargy, irritability, cardiomegaly, feeding difficulties, tachypnea, decreased energy, mild pallor, and "pica" (craving and chewing substances that have no nutritional value). A consistent finding in various studies is that iron-deficiency anemia, and especially the severe form, has negative effects on the development of immunity, neurological, cognitive, school performance and exercise tolerance that persist even after the instituted treatment [7–10]. The UK *National Screening Committee* (UK NSC) analysis noted that although iron treatment improves iron levels in young children, there is contradictory evidence of effects on long-term health or cognitive development outcomes [11]. The association between severe iron-deficiency anemia and stroke in young children has been recognized in many publications [12–16]. The association of iron-deficiency anemia and the rare and severe phenotype of thrombosis in pediatrics has clinical

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relevance. Severe iron-deficiency anemia and secondary thrombocytosis, based on animal models, are independent risk factors for the development of thrombus and its propagation [17]. Therefore, a very good knowledge of the risk factors of iron-deficiency anemia is required. These factors are maternal factors (mother's age, maternal history of anemia, mother's level of education), individual factors (age, gender, birth score), as well as environmental factors (rural/urban environment, standard of living of family). The main causes of iron-deficiency anemia are low intake of iron through food, chronic blood loss due to gastric conditions or malabsorption syndrome. In severe iron-deficiency anemia, the first-choice therapy is represented by orally administered iron preparations (sucrosomial iron, ferrous sulfate or gluconate) that have high intestinal absorption and a good efficiency/safety/cost ratio [18]. In cases of intolerance to oral treatment with iron preparations or chronic malabsorption, parenteral iron or red blood cell concentrate transfusions are recommended.

Aim

The aim of our work was to study the causes of iron deficiency, laboratory findings and clinical manifestation of infants aged 6–12 months and children aged 1–3 years old diagnosed with severe iron-deficiency anemia.

Patients, Materials and Methods

Study design

We conducted an observational, retrospective single tertiary center study between January 2015 and April 2022, which included 142 children admitted to our Clinic with severe iron-deficiency anemia. This retrospective study was performed in the Department of Pediatrics, Emergency County Clinical Hospital of Craiova, Romania, under the approval of the Institutional Review Board and Ethics Committee of Publication (Approval No. 15630/29.03.2023). Before the inclusion in the study, the guardians of the children were informed about the protocol, and they gave their consent for the use of the data for research purposes. Clinical data were retrospectively collected from Hospital medical records. For each patient, we recorded the following information: mother's age at birth, mother's level of education, gestational age (GA), birth weight (BW), nutrition from birth to admission, living conditions, age and weight at admission, prophylaxis of iron-deficiency anemia, causes of severe iron-deficiency anemia, associated deficiency diseases, clinical manifestations, cardiovascular (CV) manifestations, paraclinical investigations (complete blood count, serum iron, serum ferritin) and administered treatment.

Study population

The cohort group in the study comprises 142 children aged 6–36 months referred to at our Pediatrics Clinic. The cohort was divided into two groups. Therefore, the first group, the control group (patients with no diagnosis of severe iron-deficiency anemia), included 71 patients who presented between January 2015 and April 2022 in the Department of Pediatrics, Emergency County Clinical Hospital of Craiova, for other symptoms (nausea, diarrhea, fever, abdominal pain). The study group (patients diagnosed with severe iron-deficiency anemia) included 71 patients admitted between January 2015 and April 2022 in the same Department for pallor, loss of appetite, fatigue, irritability, and underweight. Our study excluded patients with associated acute conditions that would impact the hematological profile (infectious causes, oncological diseases, trauma, and gastrointestinal bleeding).

Diagnostic tests

The following methods were used to determine the Hb value: electrical impedance and flow cytometry. A Hb value <11 g/dL was considered anemia and classified according to the *WHO* into mild (10–10.9 g/dL), moderate (7–9.9 g/dL) and severe anemia (<7 g/dL).

Electrochemiluminescence immunoassay (ECLIA) was used to determine serum ferritin, and serum iron was analyzed by spectrophotometry. Depletion of iron stores was defined as plasma ferritin <12 μg/L. The anthropometric assessment was performed by weight and height measurements. The nutritional status was classified using the *WHO* program. Each individual's height/weight ratio was compared to the mean for the population. Therefore, nutritional status was divided into three categories. Thus, if an individual's ratio was lower than 2 standard deviations (SDs) from the mean, he was considered malnourished; if the value ranged from 2 and 2 SDs, he was considered normal, and if the height/weight ratio measured above 2 SDs, he was considered overweight. The classification of malnutrition (Gomez classification) was based on weight-for-age, representing the estimated weight/ideal weight ratio. Grade I malnutrition is defined as weight-for-age between 0.89–0.76 and a weight deficit of 10–25%, grade II malnutrition is defined as weight-for-age between 0.75–0.611 and a weight deficit between 25–40%, and grade III malnutrition is defined as weight-for-age less than 0.6 and a weight deficit greater than 40%.

Statistical analysis

To process data for the statistical analysis, Microsoft Excel was used to sort and code the quantitative and qualitative information. Statistical analysis was conducted using Statistical Package for the Social Sciences (SPSS) 25.0 (IBM, Chicago, IL, USA) software. The descriptive statistics for all the data were presented in each section. The Lilliefors test assessed the normality of measured data. The data of normal distribution were expressed as mean and SD. The data of non-normal distribution were described as a median and interquartile interval. The numerical data were defined as several cases (n) and percentages (%). Student's t-test or χ^2 (*chi*-squared) test were used to compare the differences between groups. A p-value of less than 0.05 represents statistical significance. The Pearson's correlation coefficient assessed the statistical relationship and association between variables.

Results

Twenty-two infants aged 6–12 months and 49 children aged 1–3 years admitted with severe iron-deficiency anemia in the Pediatrics Clinic, Emergency County Clinical Hospital of Craiova, were included in the study. The children had no associated conditions causing severe iron-deficiency

anemia. In the study group, infants and children were predominantly male from rural areas (Figure 1, A and B).

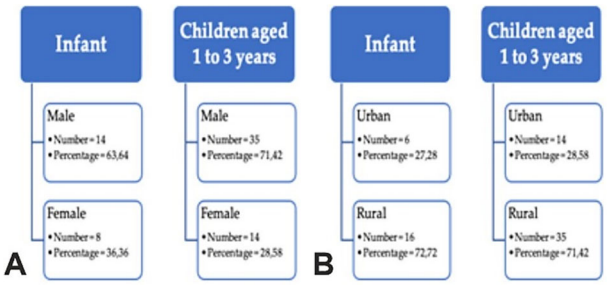

Figure 1 – ***(A) Distribution of children with severe iron-deficiency anemia by gender; (B) Distribution of children with severe iron-deficiency anemia by rural/ urban environment.***

The study group was compared to the control group. Qualitative variables were statistically tested using the *chi*-squared test. In both the study and control groups, the male gender was slightly more prevalent, but no statistically significant difference was observed regarding gender (*chi*-squared value 2.4038, p=0.121044). More patients from the study group are rural residents (51 rural, 20 urban) compared to the control group (34 rural, 37 urban). The result was statistically significant (*chi*-squared value 8.4702, p=0.00361).

Regarding the nutritional status, 29 children from the study group were dystrophic, compared to three children from the control group. In this group, 61 patients were normoponderal and seven patients were overweight. The result was statistically significant (*chi*-squared value 26.7961, p<0.01) (Figure 2).

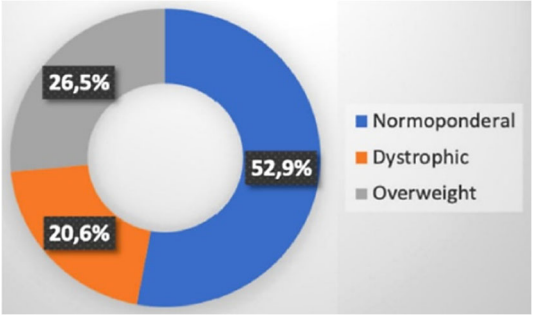

Figure 2 – ***Nutritional status of infants and children with severe iron-deficiency anemia.***

Mother's age at birth in the study group was lower on average by two years compared to the control group (Table 1). This result was deemed statistically significant (p<0.01).

Table 1 – ***Frequency of anemia cases by mother's age***

Mother's age	Control group	Study group
15–20 years	9.86%	30.99%
21–30 years	76.06%	54.93%
Over 30 years	14.08%	14.08%
Mean ± standard deviation [years]	26.8±3.9	24.3±6.2

The percentage of mothers ≤20 years old was higher in the study group (over 30%) compared to the control group (9.86%). 76.06% of mothers from the control group and 54.93% of the mothers from the study group were aged between 21–30 years, while the percentage is the same in both groups for mothers age over 30. Using Pearson's correlation test, we found a significant positive correlation between mothers aged ≤20 years and the number of anemia cases. Negative correlations were observed between the mothers aged >20 years and the number of anemia cases.

In the study group, mothers' level of education varied, with the highest share going to mothers with middle school education – 77.96% (ranging from 2 to 8 grades), then to mothers with high school education – 15.25%, and finally to mothers with higher education –6.79%. Education, an indirect indicator of living standard, presents a statistically significant difference between the two groups (*chi*-squared value 39.0108, p<0.01). Higher education levels are prevalent in the control group compared to the study group.

Living standard was significantly lower in the study group compared to control group (*chi*-squared value 63.029, p<0.01). In the study group, low living standard was observed in 76.06% of patients, average living standard was observed in 16.9% of patients, and adequate living standard was observed in 7.04% of patients (Tabel 2).

Table 2 – ***Living standard among study and control groups***

Living standard	Study group		Control group	
	No. of cases	*%*	*No. of cases*	*%*
Low	54	76.06	35	49.29
Average	12	16.90	28	39.43
Adequate	5	7.04	8	11.26

Marital status, a factor with multiple indirect significations, was statistically different between the two groups (*chi*-squared value 7.329, p=0.006). Mothers from the study group are more likely to be not married. Birth rank shows a statistically significant distribution (*chi*-squared value 8.7014, p=0.012898). In the control group, most patients are first-born (63.38%), while in the study group the percentage is much lower (40.85%). Regarding second-born children, a higher percentage is observed in the study group (45.07%) than in the control group (32.39%). 14.08% of anemic children are third-born, *versus* only 4.23% of healthy children. Using the Pearson's correlation test, we obtained a significant negative correlation between the presence of anemia and rank 1, and a significant positive correlation between anemia and rank 3 or higher and the presence of anemia (Table 3).

Table 3 – ***Frequency of anemia cases by rank of birth***

Birth rank	Control group	Study group
Rank 1	63.38%	40.85%
Rank 2	32.39%	45.07%
Rank 3+	4.23%	14.08%

We noted a higher frequency of premature births (14.08%) in children identified with anemia compared to healthy children (8.45%). However, no significant difference between the presence of anemia in term and preterm birth was found (*chi*-squared value 1.127, p=2.8842). Also, no correlation was found using the Pearson's correlation test (Table 4).

Table 4 – ***Type of birth among control and study groups***

Birth type	Control group	Study group
Term	91.55%	85.92%
Preterm	8.45%	14.08%

We found a statistically significant distribution of cow's milk consumption among the two groups (*chi*-squared value 37.404, $p<0.001$). 67% of anemic children preferentially consumed cow's milk (67.61%) – this finding could probably correlate with rural residence and living standard. By contrast, only 16.90% of the control group consumed cow's milk. Pearson's correlation test reveals a significant positive correlation, indicating that anemia is directly proportional to cow's milk consumption (Table 5).

Table 5 – *Cow's milk consumption among control and study groups*

Cow's milk	Control group	Study group
Consumption	16.90%	67.61%
No consumption	83.10%	32.39%

The causes of anemia among infants aged 6 to 12 months were premature birth in 10 infants, gemellarity for eight infants, feeding of powdered cow's milk to 14 infants, inadequate diversification nutrition in eight infants, four babies had patent *ductus arteriosus*, and one infant had pulmonary tuberculosis (Table 6).

Table 6 – *Causes of severe iron-deficiency anemia in infants aged 6–12 months*

Cause	No. of cases
Premature birth	10
Twinhood	8
Bottle feeding with cow's milk	14
Incorrect food diversification	8
Patent *ductus arteriosus*	6
Pulmonary tuberculosis	1

Among children aged 1 to 3 years, the most frequent causes were excessive cow's milk feeding (about 2 L/24 hours) for 34 children, delayed diversification through feeding for 20 children, increased consumption of starchy products reported for 10 children, six children had intestinal giardiasis and three were diagnosed with ascariasis; no prophylaxis of iron-deficiency anemia was performed for 20 children and two had anemia due to premature birth. Four children had an atrial septal defect, two had a ventricular septal defect, and one had a cleft palate (Table 7).

Table 7 – *Causes of severe iron-deficiency anemia in children aged 1–3 years*

Cause	No. of cases
Excess feeding with cow's milk (>2 L/24 hours) using nursing bottle	34
Late food diversification	20
Excess of flour products	10
Intestinal giardiasis	6
Ascariasis	3
Prophylaxis of iron-deficiency anemia was not carried out	20
Anemia due to premature	2
Atrial septal defect	4
Ventricular septal defect	2
Cleft palate	1

The clinical manifestations in children with severe iron-deficiency anemia were marked skin pallor in 48 children, capricious appetite in 26 children, pica in 14 children, inappetence in 12 children, and agitation in 10 children (Table 8).

Table 8 – *Clinical manifestations in children with severe iron-deficiency anemia*

Clinical manifestation	No. of cases
Marked skin pallor	48
Capricious appetite	26
Pica	14
Inappetence	12
Agitation	10

We carefully followed the CV manifestations of all children with severe iron-deficiency anemia upon admission. We found the presence of functional apex systolic murmur in several 60 children, tachycardia in 38 children, arterial hypotension in 12 children, deafening of heart sounds in six children and congestive heart failure in 10 children (Table 9).

Table 9 – *Cardiovascular manifestations in children with severe iron-deficiency anemia*

Cardiovascular manifestation	No. of cases
Functional apex systolic murmur	60
Tachycardia	38
Arterial hypotension	12
Deafening of heart sounds	6
Congestive heart failure	10

The diagnosis of iron-deficiency anemia has three conditions: (*1*) Hb <11 g/dL; (*2*) blood cell morphology consistent with microcytic hypochromic anemia; (*3*) iron biochemistry test shows iron deficiency.

In our study group, the mean Hb value in infants was 6.12±1.18 g/dL (3.5–7 g/dL), and in children aged 1 to 3 years, 5.89±1.13 g/dl (1.21–6.3 g/dL), with an overall mean of 5.3±1.3 g/dL.

Serum iron in infants ranged from 11.38±1.68 μg/dL (12–15 μg/dL), and in children aged 1 to 3 years was 11.81±3.21 μg/dL (5–21 μg/dL), with a total mean of 12.7±4.4 μg/dL. The hematocrit (Ht), the mean corpuscular volume (MCV), the mean corpuscular hemoglobin concentration (MCHC), and the mean corpuscular hemoglobin (MCH) had low values. The value of serum ferritin was 4.1±1.1 ng/mL. All blood variables showed significantly lower values in the anemia group than in the control group (Student's *t*-test, $p<0.001$, normality of data was checked by Lilliefors test) (Table 10).

Table 10 – *The mean values of hematological parameters in children with severe iron-deficiency anemia, and in control group*

Variables	Anemia group (mean ± SD)	Control group (mean ± SD)
Hb [g/dL]	5.3±1.3[1]	12.1±0.4
Ht [%]	19.5±5.2[1]	35.8±2.1
MCV [fL]	54±5.9[1]	78.3±2.4
MCH [pg]	15.3±5[1]	28.3±1.5
MCHC [g/dL]	24.5±4.4[1]	34.7±1.8
Iron [μg/dL]	12.7±4.4[1]	69±18.4
Serum ferritin [ng/L]	4.1±1.1[1]	90±29.9

Hb: Hemoglobin; Ht: Hematocrit; MCV: Mean corpuscular volume; MCH: Mean corpuscular hemoglobin; MCHC: Mean corpuscular hemoglobin concentration. Normal values: Ht (32–40%), MCV (70–85 fL), MCH (22–30 pg), MCHC (32–38 g/dL), Iron (female: 33–170 μg/dL; male: 43–176 μg/dL), Serum ferritin (14–152 ng/mL). [1]SD: Standard deviation.

The examination of the peripheral blood by the blood smear assay, using the May-Grünwald–Giemsa technique,

revealed the predominant presence of small red blood cells (microcytosis), with hypochromia, or inhomogeneously stained (polychromatophilia), which shows the reduction of the amount of Hb. Other times, the red blood cells had an irregular outline, with varying lengths (poikilocytosis) or particular shapes (pencil or sickle shaped) (Figure 3).

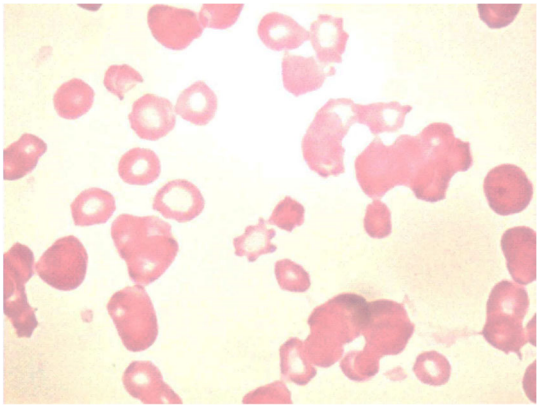

Figure 3 – ***Peripheral blood smear showing the presence of small red blood cells (microcytes), hypochromic or inhomogeneously stained, deformed, with extensions of various shapes, in a patient with iron-deficiency anemia. May-Grünwald–Giemsa staining, ×1000.***

Of the 71 children with severe iron-deficiency anemia, 10 received oral iron treatment and age-appropriate dietary recommendations, 57 children received transfusions of red blood cell concentrate, leukocyte-depleted from donors with the same blood group and Rh, six children required two transfusions each, and four children had blood group and Rh incompatibility with the donor blood on multiple tests. They were given universal donor – 0 negative (Table 11).

Table 11 – ***The treatment regimens used to children with severe iron-deficiency anemia***

Treatment	No. of cases	%
Oral treatment	10	14.08
Transfusion of red blood cell concentrate, leukocyte-depleted from donors with the same blood group and Rh	57	80.28
Incompatibility blood group and Rh	4	5.64

Discussions

Children hospitalized with severe iron-deficiency anemia come from Dolj County (south-west region of Romania) and neighboring counties. In the study, the male sex predominated in infants (63.64%) and children aged 1–3 years (71.42%), as also found in published articles. The predominance in boys may be genetically determined or may reveal an increased incidence of iron deficiency in boys [19–21].

In Lundblad's study, 61% of affected children with iron-deficiency anemia were female [22], but there are articles demonstrating no significant gender differences in children with iron-deficiency anemia [23]. Most infants (72.72%) and children aged 1–3 years (71.42%) came from rural areas, where the level of education is lower, and household income is more limited. Studies have shown that anemia is more prevalent among disadvantaged classes with fewer years of schooling, lower family income, and a place of residence [24, 25].

Another study showed that in rural areas, the knowledge about child nutrition is limited, family income is lower, and they must comply with regular check-ups with the family doctor [26]. Residence in rural areas and lack of knowledge about healthy nutrition are risk factors for iron-deficiency anemia [27]. In our study, most mothers had middle school education (77.96%) (we only had information on the educational level for 59 of the 71 mothers), low and average living (92.96%), and about a quarter of mothers were minors.

In young mothers (15–24 years old), there is a higher risk of anemia in their children [28, 29]. Lee *et al.* state that 25% of newborns whose mothers are teenagers have iron deficiency [30].

In 84.4% of the children in the study, iron-deficiency anemia prophylaxis was not performed or was partially completed.

Most children, both infants, and children aged 1 to 3 years, had nutritional causes as the primary origin of severe iron-deficiency anemia, the most common of which was feeding with cow's milk (up to 2 L/24 hours), bottle-fed both day and night, often with added flour products. Severe iron-deficiency anemia in children who consume large amounts of cow's milk by nursing bottle results in failure to regulate milk intake [31–33]. Cow's milk at young ages has adverse effects on iron stores. It promotes anemia, can cause ocular hemorrhages (40% of healthy infants and young children), inhibition of iron absorption, calcium, and casein in large amounts, and renal load [34, 35]. Apart from dietary causes, other causes that determine severe iron-deficiency anemia in infants were premature birth, twinhood, patent *ductus arteriosus*, and pulmonary tuberculosis. Other causes that determine the occurrence of severe iron-deficiency anemia in children aged 1–3 years were intestinal giardiasis, ascariasis, prophylaxis of iron-deficiency anemia incompletely carried out, atrial septal defect, ventricular septal defect, and cleft palate.

McCarthy *et al.* describe in their article the following: high consumption of cow's milk can replace solid food sources rich in iron, and increased intake of cow's milk is associated with low serum ferritin concentration after the age of two years [36]. We have also encountered dietary diversification errors (early/late diversification with non-age-appropriate foods).

Delayed clamping of the umbilical cord up to 1–3 minutes after birth facilitates placental transfusion and blood flow to the newborn. It is a low-cost or no-cost intervention to reduce early anemia [37–39].

According to the latest data published by the *National Institute of Public Health* in Romania, the exclusive breastfeeding rate is 12.6% (among the lowest in Europe). The dynamics show a decrease in exclusive breastfeeding in the last two years. Variations are essential in the country's different regions; the lowest rate of exclusive breastfeeding, around 10%, is found in Muntenia, Banat, and Oltenia – the area where the children in this study come from [40]. In addition to the fact that we are in a place where exclusive breastfeeding has a low incidence, there are also these dietary mistakes, excessive use of cow's milk with flour products (probably preserving past nutritional habits) and diversification mistakes. Shalby *et al.* reported two cases in Saudi Arabia with shallow Hb values (1.1 g/dL and 1.2 g/dL);

this study states that such cases are not found in the specialized literature [41].

During the study, six children were hospitalized with Hb values between 1.2 g/dL and 1.84 g/dL. We present the case of a one year and 10 months old girl with the lowest Hb value (1.2 g/dL), weighing 9 kg, who was admitted in March 2022 with her mother for severe pallor. Personal, physiological, and pathological history were the eighth child born to his mother from twin pregnancy, GA 38 weeks, BW 2700 g, Apgar score 9, breastfed until eight months of age, then continued exclusively with cow's milk until admission, diversification was incomplete with deficiencies, rickets prophylaxis with vitamin D_3 was not performed, a dental eruption at one year of age, diagnosed with psychomotor retardation one month before admission. General condition on admission was as follows: severe general condition, afebrile, lethargic, poor nutritional status, intensely pale integuments, obvious signs of rickets, polypnea, precordial grade III systolic murmur, blood pressure 93/63 mmHg, heart rate 140 bpm, liver palpable 3 cm below the costal margin, no signs of meningeal irritation. Corroborating the clinical data, the girl presented, in addition to the clinical manifestations of severe iron-deficiency anemia and congestive heart failure. The results of the laboratory tests were Hb 1.2 g/dL, Ht 5.53%, MCV 51.05 fL, MCH 11.19 pg, serum iron 5 μg/dL, serum ferritin 2.27 ng/mL, calcium 7.8 mg/dL. The child received two transfusions of red blood cell concentrate, leukocyte depleted. Discharge recommendations: the mother was explained how to ensure the correct nutrition of the child and was also advised to continue oral iron treatment. In the case of these children, probably neither the health care in their localities supervised them, the social worker, nor the local community could observe the situation of these children. Cow's milk consumed in large quantities every day can jeopardize their future. Most children showed marked pallor, capricious appetite, pica, and restlessness. Patients with severe iron-deficiency anemia also presented, at admission, one or more CV manifestations, among which we mention: functional apex systolic murmur, tachycardia, and in very severe cases, arterial hypotension, deafening of heart sounds, and congestive heart failure. A study published in 2022 mentioned that iron deficiency could lead to critical cardiac manifestations, such as systolic or diastolic dysfunctions and arrhythmias. However, there are limited studies on iron deficiency's effect on children's CV function [42]. 70.84% of children with severe iron-deficiency anemia in our study had deficiency rickets, with mean serum calcium values of 8.3±0.42 mg/dL (7.2–8.8 mg/dL). 52.9% of children were average weight, 20.6% were dystrophic, and 26.5% were overweight. Severe iron-deficiency anemia was also associated with overweight or obese children, as described by other authors [43, 44]. Approximately 70% of mothers did not come to the hospital on their initiative as they did not notice their children's pallor, probably also because it had set in over time; they were sent to be admitted by the hospitals they belonged to. Most children received emergency transfusion treatment. Six children received two transfusions of packed red blood cells each. Four children had blood group and Rh incompatibility with the donor at several tests, so they received transfusion treatment with a universal donor. Further, they received treatment with oral iron supplements and a correct and age-appropriate diet.

Brain growth is higher in the first two years of life, when the central nervous system membranes are more permeable to iron, representing the most critical time for its use. Iron deficiency has consequences such as losing physical and cognitive development, which impairs learning ability and decreases work capacity [45].

Promoting better nutrition in the first 1000 days of life has been one of the strategies to improve health status in adulthood and human development. It reinforces the importance of preventing nutritional deficiencies, such as iron-deficiency anemia, in the first two years of life. Aged mothers can meet their children's health care demands more. The risk of anemia in children of younger mothers suggests that these are less ready to meet their children's nutritive requirements and perform the duties of parenting. This may reflect the lack of financial resources, lack of knowledge about anemia and childcare, and lack of adequate guidance.

Study limitations

Regarding the limits of this study, we state that we did not have data on the child's nutrition, on the quality and quantity of food consumed, data that are important to better understand the causes of childhood anemia. Anemia, a result of food instability in the children's lives, reflects the violation of the right to regular and endless access to quality food in sufficient quantity. Factors associated with anemia are also the socio-economic and behavioral conditions of the population, which have a direct impact on the nutrition and health of these individuals.

Due to the small number of patients in the last three years, some tests (urinary hepcidin, free erythrocyte protoporphyrin, transferrin, total iron binding capacity) were not performed in a hospital; it was not possible to specify the level of education of all mothers because this study was retrospective, it was not possible to calculate the incidence of severe iron-deficiency anemia because in the last three years of the study, period coincided with the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection when admissions were few, predominantly emergencies.

Conclusions

Children with severe iron-deficiency anemias concern us; they are often emergencies, sometimes life-threatening. The most frequent cause of iron-deficiency anemia in infants and children 1–3 years old was the consumption of cow's milk following incorrect diversification and incomplete prophylaxis of iron-deficiency anemia. The male gender was slightly more prevalent. We believe it is necessary to expand public health actions for education to understand the severity and consequences of severe iron-deficiency anemia and to prevent the occurrence of anemia through a correct diet, corresponding to the child's age. It is much easier to feed a child correctly than to reach the transfusion treatment.

Conflict of interests

The authors declare no conflict of interests.

Institutional Review Board Statement

The study was conducted by the Declaration of Helsinki and approved by the Institutional Review Board (or Ethics Committee) of the Emergency County Clinical Hospital of Craiova, Romania (Approval No. 15630/2023, March 29).

Informed Consent Statement

Informed consent was obtained from all subjects involved in the study. Written informed consent has been obtained from the patient's tutors to publish this paper.

Acknowledgments

This study was supported by internal Grant No. 26/1031/2022, October 8, "Clinical and therapeutic aspects in severe iron deficiency anemia in infants and young children" of the University of Medicine and Pharmacy of Craiova, Romania.

Authors' contribution

Cristina Elena Singer and Viorel Biciuşcă equally contributed to the manuscript and share main authorship.

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Received: August 29, 2023

Accepted: October 18, 2023