Iron Profile in Patients with Congenital Cyanotic Heart Disease

Running Title: Congenital Cyanotic Heart Disease

Ghada Omar El-Sedfy [1], Ahlam Badwy Ali [1], and Esraa Sami Abd El-Rahman [*]
Department of Pediatrics, Faculty of Medicine, Assiut University, Egypt.
Corresponding author: E-mail: esraasami225@gmail.com

Abstract

Background: Congenital cyanotic heart disease (CCHD) patients experience hypoxia, which stimulates erythropoiesis and polycythemia, increasing iron consumption and depleting iron reserves. The ensuing iron deficiency anemia (IDA) is made worse by hype viscosity because microcytic erythrocytes, which are resistant to deformation in the microcirculation, are present. As a result, cyanotic episodes and cerebrovascular accidents occur more frequently. **Aim:** The present study aims to assess the iron profile and detect the prevalence of IDA in patients with CCHD admitted to the Cardiology Unit at Assiut University Children's Hospital (AUCH) for one year. **Patients and Methods:** 75 patients with CCHD participated in the one-year descriptive cross-sectional study conducted at the AUCH cardiology unit from January 1 through December 31, 2021. A complete blood count (CBC) with differential count and retics, serum iron, total iron binding capacity (TIBC), serum ferritin, and transferrin saturation were all performed on these patients. The patients with CCHD were split into groups, Group A (non-iron deficient group, n=56) and Group B (iron deficient group, n=19), based on the serum ferritin level. **Results:** The median age of the studied cases was seven months, ranging from one month and a half up to 11 years old. The older the patients with uncorrected CCHD, the more likely they will have IDA (P=0.014). According to the serum ferritin level, we divided the 75 children with CCHD into Group A (non-iron deficient group, n=56) and Group B (iron deficient group, n=19). According to their blood ferritin levels, in the current study, iron deficiency was present 25.3% of the time in children with CCHD. Serum iron and transferrin saturation, as well as Mean corpuscular volume (MCV), Mean corpuscular hemoglobin (MCH), and mean corpuscular hemoglobin concentration (MCHC), were all considerably lower in the iron-deficient group than in the non-iron-deficient group (P0.05). The median blood ferritin level of the iron-deficient group ranged from 12.0 (1.0 - 25.0) ng/mL to 106.0 ng/mL in the non-iron-deficient group (22.0 - 288.3). (P 0.001). **Conclusion:** IDA is significantly more prevalent in CCHD patients. **Keywords:** Iron; Congenital Cyanotic Heart Disease; anemia; iron deficiency anemia.

Introduction

Patients with CCHD suffering from hypoxia are associated with secondary erythropoiesis and erythropoietin production. They experience polycythaemia and hyperviscosity, which may be manifested clinically as thromboembolic episodes [(1)]. It was noticed that patients with CCHD have IDA as a prevalent problem. Some potential causes of IDA include improper venesection. Hemoptysis is characterized by hemorrhage from collateral vessels or arteriovenous malformations, inadequate hemostasis, a reduction in food intake or absorption, and the use of anticoagulants and antiplatelets (3). IDA exacerbates hype viscosity symptoms because the microcirculation contains microcytic erythrocytes that are resistant to deformation. As a result, people who have IDA are more likely to have morbidity, including cerebrovascular accidents and cyanotic episodes. Due to polycythemia, patients with (CCHD) have higher hemoglobin and hematocrit levels, making diagnosing their iron deficit more challenging (1). Additionally, clinical pallor-based anemia diagnosis in CCHD is challenging due to the presence of hypoxia

-induced polycythemia. As a result, frequent screening and laboratory tests are crucial for diagnosis (4). The relevance of detecting iron deficiency in this population is highlighted by the high occurrence of the condition among children with CCHD.

Patients And Methods

The cardiology unit at (AUCH) conducted this one-year descriptive cross-sectional study from January 1 to December 31, 2021. The current study included every child with CCHD who was admitted to the Cardiology Unit at AUCH during the study period. The study's objectives were to determine the prevalence of IDA in patients with CCHD and to evaluate their iron profiles in relation to the inclusion criteria. There were 75 CCHD patients in the research.

Inclusion Criteria: Patients diagnosed (CCHD) based on clinical signs and echocardiography, aged between one month and 18 years, who were admitted to the Cardiology Unit at the AUCH during the study period were included. Additionally, eligible patients had CCHD that had not been corrected surgically and had not received iron supplements in the past three months. Patients with CCHD were also included if they did not have other systemic diseases, such as chronic kidney disease or hemolytic anemia, which could affect iron profiles and lead to anemia.

Exclusion Criteria: Infants younger than one month (newborn), individuals with cyanotic congenital heart disease, patients who have undergone surgical correction, those who have taken iron supplements within the last three months, and individuals with other systemic illnesses that affect iron profiles and result in anemia, such as chronic kidney disease or hemolytic anemia.

Methodology:

Eligible participants who accepted to participate in the study were subjected to the following preliminary evaluation for inclusion in this study:

Personal Data: Name, age, gender, social and economic status, and history suggestive of complications such as thromboembolic manifestations or heart failure.

Complete Clinical Examination: Included a general assessment comprising vital signs and a systemic examination covering the chest, cardiac, abdominal, and neurological systems.

Blood Samples Collection: 3 mL of blood was drawn and divided: 1 ml of venous blood was drawn and put into an EDTA to measure the Complete Blood Count (CBC) with differential and reticulocyte count.

One milliliter (ml) of venous blood was drawn and placed into an EDTA blood assortment tube to evaluate the serum levels of iron, ferritin, complete iron restricting limit, and transferrin saturation. The patients with CCHD were divided into Gathering A (non-iron insufficient gathering, n=56) and Gathering B (iron lacking gathering, n=19), given the serum ferritin level. As per their blood ferritin levels, the ongoing study showed that iron deficiency was common in kids with CCHD at 25.3%. In patients with untreated CCHD, the probability of paleness expanded with patient age (P=0.014). The essentially lower serum MCV, MCH, MCHC, serum iron, serum ferritin, and transferrin immersion in the iron-lacking gathering contrasted with the non-iron-inadequate gathering, which showed the presence of microcytic cells because of the lack of iron. The RBCs and TIBCs that lacked iron gathering were essentially higher than those of the non-iron inadequate gathering. Equivalent hemoglobin levels were found in the two study gatherings. Lack of iron weakness was not entirely settled in the cases that were investigated by a serum ferritin centralization of under 12 ng/mL in youngsters under 5 years of age, 15 ng/mL in kids above 5 years of age, and 30 ng/mL in kids with disease. [(17)].

Ethical Approval: Each participant in the study provided written informed consent, which was obtained after the Assiut University Ethics Board gave the study the go-ahead. The Declaration of Helsinki, the code of ethics of the World Medical Association, was followed when conducting this research on humans.

Statistical Analysis: The SPSS version 22 program was used for all statistical

calculations (statistical software for the social sciences; SPSS Inc., Chicago, IL, USA). The frequency (number of occurrences) and relative frequencies, as well as the mean, standard deviation (SD), median, and range (percentages), were used to statistically describe data when they were not normally distributed. Winslow Mann The U test was used to compare quantitative variables because the data were not regularly distributed. A Chi-square (2) test analysis was performed to compare categorical data. An exact test was used in its place when the expected frequency was less than 5. The correlation between various variables was examined using the Pearson correlation test. P-value set at level 0.05 for significance.

Results

Table 1 shows the Demographic and clinical data of the studied cases (n=75). The median age of the studied cases was seven months and ranged from one month and a half up to 11 years old; about half of the studied cases (48.0%) aged from one month and a half up to six months, seven cases (9.3%) aged > 6 months - 1 year, 25 (33.3%) cases aged > 1 year – 6 years, and seven cases (9.3%) aged > 6 year – 12 years old.

Out of the seventy-five studied cases, 41 (54.7%) were male, and 34 (45.3%) were females, with a male-to-female ratio of 1.2:1.

Table 1 Demographic and clinical data of the studied cases (n=75)

Variable name	**N**	**(%)**
Age (years)		
- Median (range)	7 months (1.5 months – 11 years)	
Age groups		
- Birth - 6 months	36	(48.0)
- > 6 months - 1 year	7	(9.3)
- > 1 year - 6 years	25	(33.3)
- > 6 years - 12 years	7	(9.3)
Sex		
- Male	52	(69.3)
- Female	23	(30.7)
Type of cardiac lesion		
CHD with decreased pulmonary blood flow	55	(73.3)
CHD with increased pulmonary blood flow	20	(26.7)
- **Heart failure**	23	(30.7)
- **Thromboembolic event**	10	(13.3)
- Brain infarction	4	(40.0)
- Brain abscess	3	(30.0)
- Infective endocarditis	3	(30.0)

CHD: cyanotic heart disease. Quantitative data are presented as mean ± SD or median (range), and qualitative data are presented as number (percentage).

Figure 1: shows the distribution of iron profile among the studied cases. 35 cases (46.7%) had normal iron levels, and 40 (53.3%) suffered from low iron levels. Regarding serum ferritin level (ng/dl), 56 cases (74.7%) have normal serum ferritin levels, and 19 cases (25.3%) suffered from low serum ferritin levels. While 48 cases (64.0%) have normal total iron binding capacity levels, 27 cases (36.0%) have low total iron binding capacity. For transferrin saturation (%), 39 cases (52.0%) have normal transferrin saturation, and 36 cases (48.0%) have low transferrin saturation.

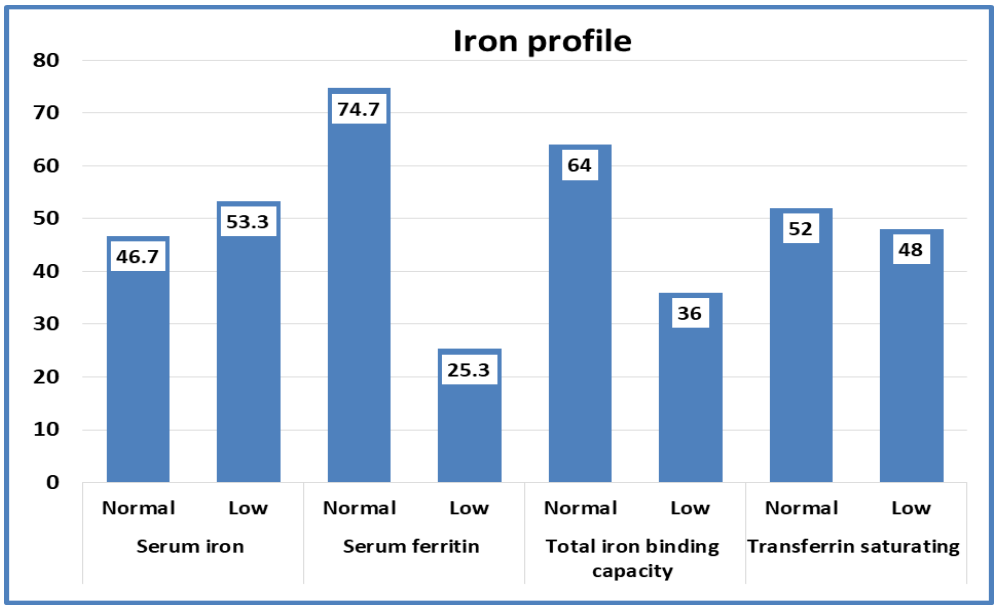

Figure 1: Bar graph showing the distribution of iron profile among the studied cases

Table 2 compares Group A (non-iron deficient group, n=56) and Group B (iron deficient group, n=19) regarding other hematological parameters and iron profile. According to the serum ferritin level, we divided the 75 children with CCHD studied into Group A (non-iron deficient group, n=56) and Group B (iron deficient group, n=19).

Table 2: Comparison of hematological parameters of iron-deficient and non-deficient group (n=75)

Hematological parameters	Group A (n=56)	Group B (n=19)	P value
WBC (*10^3/ul)	10.0 (1.1 - 19.0)	11.0 (4.2 - 17.0)	0.678
HB (g/dl)	12.9 (8.0 - 21.2)	12.9 (9.0 - 21.0)	0.421
RBCs (*10^6/ul)	5.0 (3.5 - 9.0)	7.0 (3.9 - 8.3)	0.047*
HCT (%)	42.5 (3.4 - 72.0)	51.0 (31.0 - 68.0)	0.065
MCV (fl)	80.0 (38.0 - 102.0)	68.0 (50.0 - 90.0)	0.041*
MCH (pg)	26.0 (11.5 - 42.0)	21.0 (12.0 - 31.0)	0.002*
MCHC (g/dl)	31.2 (15.4 - 38.0)	30.0 (23.0 - 35.0)	0.045*
RDW (%)	18.0 (9.4 - 29.0)	19.0 (13.2 - 26.0)	0.067
Platelets (*10^3/ul)	258.0 (92.0 - 711.0)	217.0 (135.0 - 550.0)	0.192
Retics	0.5 (0.1 - 1.1)	0.5 (0.1 - 1.1)	0.995
Serum iron (ug/dl)	82.5 (8.0 - 150.0)	20.0 (12.0 - 42.0)	<0.001*
Serum ferritin (ng/dl)	106.0 (22.0 - 288.3)	12.0 (1.0 - 25.0)	<0.001*
TIBC (mcg/dL)	251.5 (170.0 - 341.0)	300.0 (200.0 - 390.0)	<0.001*
Transferrin saturating (%)	33 (3 – 99)	7.0 (4.0 - 17.6)	<0.001*

TIBC: total iron binding capacity. Quantitative data are presented as median (range). * Significance defined by $p < 0.05$.

Discussion

Infants, who comprised more than half of the research group and had a median age of seven months, predominated (one month and a half up to 11 years old). A similar finding was reported by **Mukherjee *et al.*** [(1)], who reported that 60.8% of the 51 children with CCHD studied were less than one year old. In the current study, 13.3% of the studied CCHD children developed thromboembolic events, mainly in the form of brain infarction and brain abscess. In contrast, infective endocarditis, splenic abscess, and superior sagittal sinus thrombosis were documented in three cases. This can be attributed to the fact that to remedy the hypoxia, an increase in erythropoietin production leads to a rise in erythrocyte mass [(5).] As a result, symptoms of hyperviscosity, such as headache, dizziness, and cerebrovascular events, begin to manifest. This polycythaemia and hyperviscosity also lead RBCs to distort, cell

aggregates to form, and embolization may be observed [(1).] Further, due to the stiffness of the erythrocyte membrane, iron deficiency anemia (IDA) induces additional deformation of RBCs and has been linked to the worsening of hyperviscosity symptoms[(6)]. Based on blood ferritin levels, children with CCHD typically exhibited an iron deficiency prevalence of 25.3% in the current study. Similar findings were seen in Nairobi, where the prevalence of iron deficiency was 16.9%. [(5).] According to Olcay et al. (8) and Onur et al. (9), 52.2% and 63.6% of the population had IDA, respectively. According to a study by West et al. (1990), more than one-third of patients with CCHD exhibited iron insufficiency. However, a study by Ogunkunle [(10)] in Nigeria discovered a lower prevalence of iron deficit among children with CCHD. The current investigation's findings showed that children over one-year-old had a higher prevalence of these CCHD kids who were iron deficient. This age group may require more iron due to their rapid growth and development and low iron consumption, which may assist in explaining the situation. Children are prone to illness at this age since their immune systems are still maturing [(11).] The iron-deficient group (B), which had lower serum MCV, MCH, MCHC, serum iron, serum ferritin, and transferrin saturation than the non-iron-deficient group, was shown to have microcytic cells because of iron deficiency (A). Compared with the non-iron-lacking gathering, the RBCs and TIBC were impressively more noteworthy in the insufficient iron gathering. Hemoglobin levels, be that as it may, were practically identical between the two review gatherings. Extra help for our discoveries is given by an examination by Banu Onur et al. (13) that showed that absolute hemoglobin levels in CCHD patients were either typical, high, or marginally lower when contrasted with age-coordinated, sound people without cyanosis. In a condition known as relative paleness, the MCV, MCH, and serum ferritin are much of the time lower than those of their companions. All patients with CCHD who were iron inadequate had expanded red cell circulation width, a low MCV, and a microcytic hypochromic appearance on fringe blood spreads, as per Mukherjee et al. (1). Examinations declare that because of their changing responsiveness and particularity, standard iron inadequacy tests, for example, mean corpuscular volume, serum ferritin levels, and TSAT might be impacted by intense or proceeding with incendiary infections, hereditary polymorphisms, and sickle cell illness states [(14).]

In kids with CCHD, red platelet (RBC), hematocrit, and hemoglobin levels were not considered significant iron deficit marks (9). Analysts have likewise noticed that cyanotic patients with iron deficiency often miss the mark on expected microcytic, hypochromic, and erythrocyte qualities [(15).]

Besides the limits of inadequacy and abundance, there is no precise sign of iron status. Since ferritin is an intense stage reactant and its level ascents within sight of an intense or constant incendiary cycle, it is broadly accepted that a low serum ferritin level is the best single research center mark of iron exhaustion. The outcome should be deciphered with alertness in understanding a fundamental provocative cycle **[(16)]**.

Conclusion:

Patients with congenital cyanotic heart disease have a significant prevalence of iron deficiency. Routine screening for iron deficiency is recommended, and iron supplementation with good nutritional care should be provided to these children to enhance better outcomes.

Declarations:

Consent for Publication: I attest that all authors have agreed to submit the manuscript.

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