The Egyptian Journal of Hospital Medicine (October 2022) Vol. 89, Page 5017- 5022

Iron Deficiency in Children with Cyanotic and Noncyanotic Congenital Heart Disease

Eman Mahmoud Mohammed Elmoghazy, Mohammed Osman Hafez Ibrahim, Sulayman Nasr Ali Abdulnabi*, Nagwa Mohammed Shawky
Department of Pediatrics, Faculty of Medicine, Zagazig University, Egypt
***Corresponding author:** Sulayman Nasr Ali Abdulnabi, **Mobile**: (+20)01556599501, **E-mail:** solomovitch311@gmail.com

ABSTRACT

Background: Cyanotic congenital heart disease (CCHD) predisposes patients to iron deficiency due to compensatory secondary erythrocytosis. **Objective:** This study aimed to assess the prevalence of iron deficiency among infants and children having cyanotic and non-cyanotic congenital heart disease.

Patients and methods: This was a case-control study enrolled 30 children with congenital heart disease whether cyanotic or non-cyanotic at the Department of Pediatrics and Intensive Care Cardiology Unit, Faculty of Medicine at Zagazig University Pediatrics Hospital. They divided into 15 cyanotic and 15 non-cyanotic congenital heart disease. In addition, 15 healthy age- and sex-matched children were included as a control group ranged from 1 to 5 years ago. Children were investigated by doing complete blood count, pulse oximetry, erythrocyte indices and iron profile, based on the transferrin saturation.

Results: Iron deficiency anemia was found among 7 (53.3%) patients with CCHD, 2 (13.3%) patients with non-cyanotic congenital heart disease and 5 (33.3%) healthy children. There was no statistically difference between CCHD children, non-cyanotic congenital heart disease children and normal healthy children.

Conclusion: Iron deficiency anemia remains a very common health problem and leads to high morbidity and mortality rates among children with congenital heart disease.

Keywords: Congenital heart disease, Iron deficiency anemia, CCHD, Heart Disease.

INTRODUCTION

Structures of the heart or intrathoracic great vessels that are aberrant during foetal development are referred to as congenital heart disease (CHD). The most prevalent birth defect and the main factor in the death of children with congenital abnormalities is CHD [(1)]. Noncyanotic CHD and cyanotic CHD, commonly known as critical congenital heart disease are two subtypes of CHD [(2)].

There are many types of congenital heart defects. If the defect lowers the amount of oxygen in the body, it is called cyanotic. If the defect doesn't affect oxygen in the body, it is called acyanotic [(1)].

In recent literature, critical congenital heart disease can be further classified into 3 different types of lesions: right heart obstructive lesions, left heart obstructive lesions, and mixing lesions [(3,4)].

Acyanotic congenital heart diseases or left-to-right shunting lesions are the most common form of congenital heart disease. Although most resolve spontaneously, many will remain hemodynamically significant, particularly in the premature infant. Understanding the difference in pathophysiology, diagnosis, and management between the term and preterm infant is imperative to minimize the risk of secondary organ dysfunction and ensure proper growth and development [(5)].

Cyanotic congenital heart disease (CCHD) is congenital heart also defect with right to left shunting of desaturated blood. This results in decreased oxygen saturation in the systemic circulation which acts as a trigger for increase in erythropoietin production and secondary erythropoiesis in an effort to maintain tissue oxygenation [(2)]. The resultant polycythemia and hyperviscosity manifests clinically as thromboembolic events in the children with CCHD [(6)].

CCHD is usually isolated and sporadic, but it can also be associated with genetic syndromes. Approximately 15% to 20% of infants with CCHD are related to known chromosomal abnormalities. Globally, an estimate of 8 defects per 1000 live births is reported [(7,8)].

CCHD predisposes patients to iron deficiency due to compensatory secondary erythrocytosis [(9)]. The presence of iron deficiency anemia (IDA) in these children further increases their chances of morbidity in the form of cerebrovascular events and cyanotic spells [(10)]. However, the clinical detection of anemia based on pallor is hampered by the occurrence of hypoxia-induced polycythaemia in CCHD [(11)]. Laboratory tests and periodic screening are therefore mandatory for diagnosis [(12)].

This study aimed to assess the prevalence of iron deficiency among infants and children having cyanotic and non-cyanotic congenital heart disease.

PATIENTS AND METHODS

This was a case-control study which was conducted at the Department of Pediatrics and Intensive Care Cardiology Unit, Faculty of Medicine at Zagazig University Pediatrics Hospital from June to November 2021. The study included 30 children divided into 15 cyanotic and 15 non-cyanotic congenital heart disease. In addition, 15 healthy age- and sex-matched children were included as a control group.

Inclusion Criteria were: Age range 1 - 5 years. Both male and female. Children with CHD whether cyanotic or non-cyanotic.

Received: 07/06/2022
Accepted: 14/08/2022

Exclusion Criteria: Children who received blood transfusion or who did partial exchange transfusion in the past other 3 months. Children with chronic diseases other than CHD e.g. chronic hemolytic anemia and chronic kidney disease. Children who received iron supplements in previous three months. Children who have another systemic disease that affect iron profile.

All subjects who enrolled in the study were subjected to full history taking and clinical examination. Arterial blood oxygen saturation was measured by pulse oximeter.

Children were Laboratory investigated by doing Complete blood count (CBC). Erythrocyte indices included Packed Cell Volume (PCV), Haemoglobin (Hb), Haematocrit (Hct), Mean Corpuscular Volume (MCV), Mean Corpuscular Haemoglobin (MCH) and Red Cell Distribution Width (RDW).

Serum iron and ferritin levels were assessed using spectrophotometric measurements. Ferritin range was >12 ng/ml. Unsaturated iron-binding capacity (UIBC) was determined by adding ferrous iron ions to the serum so that they would bind to transferrin at unsaturated binding sites [(13)]. Total iron binding capacity (TIBC) is equal to UIBC plus serum iron.

Transferrin saturation is equal to (TIBC / serum iron) x 100. Transferrin saturation of <16% was categorized as iron deficient, and >16% was categorized as iron sufficient. Children in both the case and control groups underwent venepuncture performed according to the guidelines of World Health Organization (WHO) [(12)].

Ethical considerations:

The permission for the study was received from the Pediatrics Departments of Zagazig University Hospitals after the permission of the Institutional Review Board (IRB). Written Informed consent was taken from the patient parents and/or their caregivers. The research was carried out in compliance with the Code of Ethics of the World Medical Association (Decleration of Helsinki) for studies involving humans.

Statistical Analysis

The collected data were coded, processed and analyzed using the SPSS (Statistical Package for Social Sciences) version 22 for Windows® (IBM SPSS Inc, Chicago, IL, USA). Data were tested for normal distribution using the Shapiro Walk test. Qualitative data were represented as frequencies and relative percentages. Chi square test ($\chi 2$) to calculate difference between two or more groups of qualitative variables. Quantitative data were expressed as mean ± SD (Standard deviation). Independent samples t-test was used to compare between two independent groups of normally distributed variables (parametric data). P value ≤ 0.05 was considered significant.

RESULTS

Table 1 showed that there was no statistically significant difference between CCHD children, non cyanotic congenital heart disease children and normal healthy children regarding to sex, age, consanguinity and positive family history.

Table (1): Demographic characteristics of studied groups; cyanotic congenital heart disease children, acyanotic congenital heart disease children and normal healthy children

Variables	Cyanotic N=15	Acyanotic N=15	Control groups N=15	$\chi 2$	P-value
Sex n. (%)					
Males	7 (46.7%)	6 (40%)	10 (66.7%)	2.31	0.32
Females	8 (53.3%)	9 (60%)	5 (33.3%)		
Age					
<5 years	10 (66.7%)	14(93.3%)	9 (60.0%)	4.77	0.092
≥5 years	5 (33.3%)	1 (6.7%)	6 (40.0%)		
Consanguinity (%)					
Yes	2(13.3%)	4(26.7%)	0(0.0%)	4.61	0.099
No	13(86.7%)	11(73.3%)	15(100%)		
Family history (%)					
Positive	2(13.3%)	4(26.7%)	0(0.0%)	4.61	0.099
Negative	13(86.7%)	11(73.3%)	15(100%)		

χ 2=chi square test of significant **, P** >0.05 insignificant

Table 2 showed that there was no statistically difference between CCHD children, acyanotic congenital heart disease, healthy children regarding hemoglobin level, blood indices.There was statistically significant difference between studied groups regard their RDW.

Table (2): Hemoglobin and blood indices of studied groups; cyanotic congenital heart disease children, a cyanotic congenital heart disease children and normal healthy children.

Variables	Studied groups						χ^2	P-value
	Cyanotic N=15		Acyanotic N=15		Control groups N=15			
	No.	%	No.	%	No.	%		
Hemoglobin (g/dl)								
Iron deficiency	0	0.0	3	20	4	26.7	4.39	0.11
Normal	15	100	12	80	11	73.3		
MCV								
Iron deficiency (<75F/L)	6	40	6	40	6	40.0	0	1
Normal(75-100 F/L)	9	60	9	60	9	60.0		
MCH (pg)								
Iron deficiency (>23pg)	5	33.3	3	20	4	26.7	0.68	0.74
Normal (≥23 pg)	10	66.7	12	80	11	73.3		
MCHC								
Iron deficiency (<31 g/dl)	5	33.3	3	20.0	4	26.7	0.68	0.74
Normal (31 -36 g/dl)	10	66.7	12	80.0	11	73.3		
RDW								
Iron deficiency (>14.5%)	13	86.7	3	20.0	4	26.7	16.4	0.0001
Normal (11-14.5%)	2	13.3	12	80.0	11	73.3		
Hematocrit								
Iron deficiency (<34%)	0	0.0	7	46.7	7	46.7	10.2	0.006
Normal (34 %-60%)	15	100	8	53.3	8	53.3		

MCV: mean corpuscular volume**, MCH:** mean corpuscular hemoglobin, **MCHC:** mean corpuscular hemoglobin concentration**, RDW:** red cell distribution width**,** χ^2: Chi-square test of significant**, P**>0.05 insignificant**, P**≤0.05 significant.

Table 3 showed that there no statistically difference between CCHD, acyanotic congenital heart disease, healthy children regarding serum ferritin level of iron deficiency. Whereas Ferritin Risk iron deficiency anemia significantly higher in CCHD, acyanotic congenital heart disease children compared to normal children. While studied normal children had significant normal Ferritin level.

Table (3): Serum ferritin, Ferritin grade of studied groups; cyanotic congenital heart disease children,a cyanotic congenital heart disease children and normal healthy children

Variables	Cyanotic N=15		Acyanotic N=15		Control groups N=15		χ^2	P-value
	No.	%	No.	%	No.	%		
Serum ferritin								
Iron Deficient	5	33.3	3	20	4	26.7	0.68	0.71
Iron sufficient	10	66.7	12	80	11	73.3		
Ferritin grade								
Iron deficiency	5	33.3	3	20	4	26.7		
Depletion iron storage (12-50ng/L)	3	20.0	3	20	0	0.0	22.4	0.001
Risk iron deficiency anemia (>50-100 ng/L)	7	46.7	9	60	3	20		
Normal (>100 ng/L)	0	0.0	0	0.0	8	53.3		

χ^2: Chi-square test of significant**, P**>0.05 insignificant**, P**<0.05 significant, Iron deficient: (serum ferritin saturation <12 ng/L, if child <5 years or <15ng/L if child ≥5 years), Iron sufficient: (serum ferritin saturation ≥12 ng/L if child <5 years or ≥15ng/L if child ≥5 years).

Table 4 showed that there wasno statistically difference between CCHD children, acyanotic congenital heart disease, healthy children regarding to transferritin saturation percent.

Table (4): Trans ferritin saturation% of studied groups; cyanotic congenital heart disease children, a cyanotic congenital heart disease children and normal healthy children

Variables	Cyanotic N=15	Acyanotic N=15	Control groups N=15	χ^2	P-value
Trans ferritin saturation%					
Iron deficient	8 (53.3%)	6(40.0%)	4 (26.7%)	2.22	0.33
Iron sufficient	7 (46.7%)	9(60.0%)	11 (73.3%)		

χ^2: Chi-square test of significant**, P**>0.05 insignificant, Iron deficient: (Trans ferritin saturation <16%), Iron sufficient : (Trans ferritin saturation ≥16%).

Table 5 showed that there was no statistically difference between CCHD children, acyanotic congenital heart disease, healthy children regarding to prevalence of deficiency anemia.

Table (5): Iron deficiency anemia of studied groups; CCHD children, acyanotic congenital heart disease children and normal healthy children.

Variables	Cyanotic N=15	Acyanotic N=15	Control group N=15	χ^2	P-value
Iron deficiency anemia					
Yes	5 (33.3%)	3 (20%)	4 (26.7%)	0.68	0.71
No	10 (66.7%)	12 (80%)	11 (73.3%)		

χ^2: Chi-square test of significant**, P**>0.05 insignificant, Iron deficient anemia: (serum ferritin <12 ng/L if child <5 years or <15ng/L if child ≥5 years & Transferritin saturation <16%), normal: (serum ferritin ≥12 ng/L if child <5 years or ≥15ng/L if child ≥5 years & Trans ferritin saturation ≥16%).

Table 6 showed that all studied group had iron deficiency level of blood indices and iron parameters. There was significant normal Hemoglobin level and Hematocrit level in anemia CCHD children, compared to acyanotic congenital heart disease children and normal children.

Table (6): Compared blood indices, iron parameters of iron deficiency children of studied groups

Variables	Serum ferritin of anemia among studied groups						χ^2	P-value
	Cyanotic N=5		Non cyanotic N=3		Control groups N=4			
	No.	%	No.	%	No.	%		
Hemoglobin (g/dL)								
Iron deficiency	0	0.0	3	100	4	100	12	0.002
Normal	5	100	0	0.0	0	0.0		
MCV								
Iron deficiency (<75F/L)	4	80	3	100	4	100	1.5	0.47
Normal(75-100 F/L)	1	20	0	0.0	0	0.0		
MCH (pg)								
Iron deficiency (>23pg)	5	100	3	100	4	100	-	-
MCHC								
Iron deficiency (<31 g/dl)	5	100	3	100	4	100	-	-
RDW								
Iron deficiency (>14.5%)	5	100	3	100	4	100	-	-
Hematocrit								
Iron deficiency (<34%)	0	0.0	3	100	4	100	12	0.002
Normal (34 %-60%)	5	100	0	0.0	0	0.0		
Serum iron (mg/dl)								
Iron deficiency (<50 mg/dl)	5	100	3	100	4	100	-	-
TIBC								
Iron deficiency (>450 mg/dl)	5	100	3	100	4	100	-	-
UIBC								
Iron deficiency (>340 mg/dl)	5	100	3	100	4	100	-	-

χ^2: Chi-square test of significant**, P**>0.05 insignificant**, P**<0.05 significant.

DISCUSSION

In our study, there was no statistically difference between CCHD, acyanotic congenital heart disease children and normal healthy children regarding to sex, age, consanguinity and positive family history.

Ossei *et al.* [11] determined the occurrence of CHD in children below 15 years and assessed the prevalence of relative iron deficiency anaemia. Eighty (females: 44, males: 36) cases of CHD were recorded. Fifty percent of the cases occurred in children from birth to less than a year, 38.8% occurred in those aged 1–5 years and 11.3% of the cases were in children over 5 years.

In the present study, there were no statistically differences between CCHD children, acyanotic congenital heart disease and healthy children regarding to hemoglobin level and blood indices. There was a statistically significant difference between studied groups regarding their RDW and hematocrit. CCHD had higher RDW than other groups. However, hematocrit level in CCHD children was normal.

Iron deficiency anaemia was largely diagnosed using Red Cell Distribution Width (RDW) and Mean Corpuscular Volume (MCV), affordable validated parameters for diagnosing iron deficiency. When RDW and MCV are considered together, iron deficiency anemia could be diagnosed with 98% accuracy [14].

Miyamoto *et al.* [15] investigated whether RDW is associated with cardiovascular mortality after adjustment for anemia and evaluated the relationships among anemia, IL-6, and RDW in patients with ACHD. They concluded that RDW, an inexpensive clinical test, is nevertheless a powerful diagnostic predictor of cardiovascular mortality.

Soni *et al.* [16] found that the mean hemoglobin in cyanotic heart disease cases was 13.39 (SD 2.38) gm/dl. In the control group the mean hemoglobin was 9.57 (SD 1.29) gm/dl, indicating a statistically significant increased hemoglobin levels in CCHD cases.

Ossei *et al.* [11] found that of the 80 children with CHD, 66 had full blood count (FBC) carried out. Erythrocyte indices recorded were Hb, RBC, MCV, RDW, PCV and MCHC. Thirty children had Hb levels above the maximum considered normal (14.0 g/dL) and 11 had Hb values below the lower limit of 11.0 g/dL. Though the median Hb value (13.6 g/dL), was normal, there was a wide inter-patient variability with haemoglobin content of RBCs ranging from a minimum of 8.0 to to maximum of 24.3 g/dL (interquartile range, 11.0–18.7). ;

Regarding ferritin, **Olcay *et al.*** [17] in Turkey in his study to compare hematological parameters between iron sufficient and iron deficient cyanotic heart disease patients found mean ferritin to be 37.2 ng/ml in iron sufficient group and 7.5 ng/ml in iron deficient group. **Onur *et al.*** [18] in Ankara, Turkey found mean ferritin to be 39.2 ng/ml. **Lang'o *et al.*** [19] in Kenya found mean ferritin to be 48.9 ng /ml.

Soni *et al.* [16] found that mean ferritin in cases was 41.63 (SD 35.04) ng/ml and in controls it was 78.75 (SD 51.40) ng/ml with, indicating a statistically significant decreased ferritin in cases.

In our study, there was no statistically difference between CCHD children, acyanotic congenital heart disease and healthy children regarding to transferritin saturation percent. **Binh *et al.*** [20] notified that serum transferrin was higher in patients with iron deficiency but it showed a wide range of variation. **Amoozgar *et al.*** [21] demonstrated that serum iron concentrations and serum transferrin are more prone to be affected by acute disease processes and/or infection than serum ferritin and serum ferritin should be the test of choice in diagnosis of IDA.

In our study, ferritin risk iron deficiency anemia was significantly higher in CCHD children, acyanotic congenital heart disease children compared to normal children. Regarding prevalence of IDA, it was detected among 5 (33.3%) patients of CCHD, 3 (20%) patients of acyanotic congenital heart disease children and 4 (26.7%) healthy children. Statistically, there was no statistically difference between CCHD children, acyanotic congenital heart disease and healthy children regarding to prevalence of deficiency anemia. **Drossos *et al.*** [22] examined a total of 38 CCHD children and found an iron deficiency prevalence of 12.5% in children 6 to 12 years of age. Children less than five years still contributed the bulk of the iron deficiency group with a prevalence of 37.5%.

Abbod and Ibraheem [23] determined the incidence of anemia in children with CCHD by noninvasive, inexpensive, and easy laboratory methods and concluded that anemia is common in CHD patients attending hospital. Anemic CHD patients have a 3-fold increased mortality risk. Screening for anemia should be part of the routine assessment of CHD patients for risk stratification, and for treatment, when correctable causes are identified. **Ossei *et al.*** [11] concluded that CHD is a common phenomenon among newborns. Use of iron supplementation was suboptimal. Compliance with guidelines on the use of iron as well as structures for early detection of CHD for definitive interventions are advocated.

In our study, all studied group had iron deficiency level of blood indices, and iron parameters of studied groups. There was significant normal Hemoglobin level and hematocrit level in anemia CCHD children, compared to a cyanotic congenital heart disease children and normal children.

Our study stresses on the fact that IDA is a relative iron deficiency state. Hemoglobin may be normal but red blood cells are microcytic hypochromic in nature which suggests IDA. This could be further confirmed

by ferritin levels which are relatively low than general population.

As we draw attention to the need for more routine screening for CHD in children, we do not under-estimate the complexity of diagnosing the condition and management. Therefore, we present these findings with caution as several limitations confound our results. For example, patients with history of recent or current acute and chronic infection or vaccination or of renal disease should be excluded because of their known effects on bone marrow and iron metabolism. Similarly, patients with history or sign of liver disease or any genetic disorder, including Down syndrome or hypothyroidism should be excluded in these studies as these conditions cause macrocytosis. Other groups include children with leukemia or reticulo-cytosis and children already receiving iron supplements.

In conclusion, IDA remains a very common health problem and leads to high morbidity and mortality rates among children with CHD. Thus, both groups of cyanotic and acyanotic CHD are at a risk of IDA and depletion of body iron storage. Screening for anemia should be part of the routine assessment of CHD patients for risk stratification, and for treatment, when correctable causes are identified.

Conflict of interest: The authors declare no conflict of interest.

Sources of funding: This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Author contribution: Authors contributed equally in the study.

REFERENCES

1. **Desai K, Rabinowitz E, Epstein S (2019):** Physiologic diagnosis of congenital heart disease in cyanotic neonates. Curr Opin Pediatr., 31(2):274-283.
2. **Segura T, Gatzoulis M (2019):** Where are we with coronary artery disease for the cyanotic patient with congenital heart disease? Int J Cardiol., 277:108-109.
3. **Mohammad Nijres B, Samuel B, Vettukattil J (2019):** Subclinical atherosclerosis in patients with cyanotic congenital heart disease. Int J Cardiol., 282:44-48.
4. **Schaan C, Feltez G, Schaan B *et al.* (2019):** Functional capacity in children and adolescents with congenital heart disease. Rev Paul Pediatr., 37(1):65-72.
5. **Colombo J, McCulloch M (2018):** Acyanotic Congenital Heart Disease: Leftto-Right Shunt Lesions. NeoReviews. An Official Journal of the American Academy of Pediatrics, 19(7):375-383.
6. **Bernier P, Stefanescu A, Samoukovic G *et al.* (2010):** The challenge of congenital heart disease worldwide: epidemiologic and demographic facts. Semin Thorac Cardiovasc Surg Pediatr Card Surg Annu., 13:26-34.
7. **Dolk H, Loane M, Garne E (2011):** European surveillance of congenital anomalies (EUROCAT) working group. Congenital heart defects in Europe: prevalence and perinatal mortality, 2000 to 2005. https://pubmed.ncbi.nlm.nih.gov/21321151
8. **Van der Linde D, Konings E, Slager M *et al.* (2011):** Birth prevalence of congenital heart disease worldwide: a systematic review and meta-analysis. J Am Coll Cardiol., 58:2241-2247.
9. **Itiola A, Animasahun B, Njokanma O (2019):** Serum iron status of children with cyanotic congenital heart disease in Lagos, Nigeria. Sultan Qaboos Univ Med J., 19(4): 345-351.
10. **Ossei I, Buabeng K, Ossei P *et al.* (2020):** Iron-deficiency anaemia in children with congenital heart diseases at a teaching hospital in Ghana. Heliyon, 6: e03408. doi: 10.1016/j.heliyon.2020.e03408
11. **Rosove M, Perloff J, Hocking W *et al.* (1986):** Chronic hypoxaemia and decompensated erythrocytosis in cyanotic congenital heart disease. Lancet, 2:313-15.
12. **World Health Organization (2019):** Iron deficiency anemia: Assessment, prevention and control - A guide for programme managers. www.who.int/nutrition/publications/micronutrients/anaemia_iron_deficiency/WHO_NHD_01.3/en/.
13. **Obeagu E, Eze V, Alaeboh E *et al.* (2016):** Determination of hematocrit level and iron profile study among persons living with HIV in Umuahia, Abia State, Nigeria. J BioInnovation , 5:464-471.
14. **Sultana G, Haque S, Suktana T *et al.* (2013):** Value of red cell distribution width (RDW) and RBC indices in the detection of iron deficiency anemia. Mymensingh Med J., 22: 370-376.
15. **Miyamoto K, Inai K, Takeuchi D *et al.* (2015):** Relationships among red cell distribution width, anemia, and interleukin-6 in adult congenital heart disease. Circ J., 79:1100-1106.
16. **Soni S, Chaudhary P, Arya S *et al.* (2018):** To assess iron deficiency anaemia in patients with cyanotic heart disease compared to general population. Int J Pediatr Res., 5(5):268-272.
17. **Olcay L, Ozer S, Gurgey A *et al.* (1996):** Parameters of iron deficiency anemia in children with cyanotic heart disease. Pediatr Cardiol., 17(3):150-154.
18. **Onur C, Sipahi T, Tavil B *et al.* (2003):** Diagnosing iron deficiency in cyanotic heart disease. Indian J Pediatr., 70:29-31.
19. **Lang'o M, Githang'a J, Yuko-Jowi C (2009):** Prevalence of iron deficiency in children with cyanotic heart disease seen at Kenyatta National Hospital and Mater Hospital, Nairobi. East African Medical Journal, 86:47-51.
20. **Binh T, Suong N, Dinh N *et al.* (2018):** Iron deficiency anemia in children with congenital heart disease and the usefulness of erythrocyte indexes as a screening tool. Arch Gen Intern Med., 2(3):1-4.
21. **Amoozgar H, Soltani M, Besharati A *et al.* (2011):** Undiagnosed anemia in pediatric patients with congenital heart diseases. Iran Cardiovasc Res J., 5(2):69-70.
22. **Drossos C, Thanapoulos B, Papadimitrou A *et al.* (1981):** Incidence of anemia in congenital heart disease. Med. Surg. Pediatrics, 3:309-312.
23. **Abbod H, Ibraheem S (2019):** Anemia in patients with congenital heart diseases. Research submitted to Department of Pediatrics. College of Medicine. Al-Nahrain University, pp. 1-27. https://www.colmed-alnahrain.edu.iq/upload/res/940.pdf