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Assessing iron deficiency anaemia in paediatric congenital heart disease at a tertiary hospital in Eastern Uganda

M E Mohamoud,[1] MB ChB, MMed; **J O Richard,**[1] MB ChB, MMed; **M A Matan,**[1] MB ChB, MMed; **J Kimera,**[1] MB ChB, MMed; **E Tenywa,**[3] MB ChB, MMed, FCP; **W Muzeyi,**[2] MB ChB, MSc, MMed (Paeds Child Health)

[1] *Department of Paediatrics and Child Health, Faculty of Medicine and Dentistry, Kampala International University Western Campus, Bushenyi, Uganda*
[2] *Department of Paediatrics and Child Health, School of Medicine, College of Health Sciences, Makerere University, Kampala, Uganda*
[3] *Department of Paediatric and Child Health, Jinja Regional Referral Hospital, Jinja, Uganda*

***Corresponding author**: W Muzeyi (wanixxl@gmail.com)*

Background. Iron deficiency is among the most common nutritional deficiencies, and among children with congenital heart disease (CHD), the associated anaemia is a significant contributor to morbidity and mortality, especially in low- and middle-income countries where definitive surgery is usually inaccessible and significantly delayed. The objective of this study was to determine the prevalence of (and factors associated with) iron deficiency anaemia (IDA) among children with CHD at the paediatric cardiology clinic of a tertiary hospital in Eastern Uganda.
Methods. We conducted a cross-sectional study. A total of 140 children aged 6 months to 12 years with CHD were recruited into the study. IDA was defined as a ferritin level <15 µg/L and haemoglobin (Hb) as recommended by the World Health Organization for children: 6 months to <5 years Hb <11 g/dL; 5 to <12 years, Hb <11.5 g/dL; and 12 to <15 years, Hb <12g/dL. Logistic regression was used to determine factors associated with IDA.
Results. The majority (75.7%) of the participants had acyanotic heart lesions. The prevalence of IDA was 20.7% with a 95% CI of 14.7 - 28.3%. The prevalence of IDA was 26.5% and 18.9% among participants with cyanotic and acyanotic heart lesions, respectively. Lack of iron supplementation (OR 0.14; 95% CI 0.03 - 0.68; p=0.014) was associated with IDA.
Conclusion. Children with CHD in low-resource settings should be routinely screened for IDA and supplemented with iron when deficient.

Keywords. congenital heart disease; iron deficiency; iron-deficiency anaemia; cyanotic; acyanotic.

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A congenital heart disease (CHD) is a defect in the structure of the heart or great vessels that is present at birth.[1] CHDs are classified into cyanotic CHD lesions which allow circulation of deoxygenated blood in the systemic circulation via intracardiac or extracardiac shunting and acyanotic CHD that typically involve abnormal blood flow patterns within the heart and great vessels.[2] The incidence of CHD in different studies varies from about 4 per 1 000 to 50 per 1 000 livebirths.[3] In Uganda, ~8 300 children are born with CHDs annually.[4] Among them, isolated ventricular septal defect (VSD) is the most common, followed by patent ductus arteriosus (PDA) and atrial septal defects (ASDs). Tetralogy of Fallot (TOF) and truncus arteriosus are the most common cyanotic heart defects.[5] Children with CHD are at risk of significant morbidity and mortality, especially in Uganda, where heart surgery is significantly delayed – only 14% of children have access to definitive care within 2 years of diagnosis in rural parts of Uganda.[4,6] Children with CHDs have an increased demand for higher levels of circulating haemoglobin (Hb), which puts stress on their endogenous and dietary iron stores, causing a relative iron deficiency.[7] Children with CHD and iron-deficiency anaemia (IDA) are at increased risk of heart failure, cerebral vascular accidents, hyperviscosity, hypercyanotic spells, poor weight, and poor developmental growth.[7,8] IDA is among the most common nutritional deficiencies and a significant contributor to morbidity and mortality among children with CHD. A study[9] at a tertiary hospital in India reported the prevalence of IDA to be 47.06% among children with cyanotic CHD – in their study population, the incidence of cyanotic spells was higher in the iron-deficient group. There are currently no data on the burden of, and factors associated with, IDA among Ugandan children with CHD.

Methods

Study design and setting

We conducted a cross-sectional study at the paediatric heart clinic at Jinja Regional Referral Hospital (JRRH), which is in southeastern Uganda, ~87 km east of Kampala, the capital city of Uganda. JRRH is one of 13 regional referral hospitals in Uganda. It is the largest hospital in eastern Uganda, with a bed capacity of 600. The paediatric cardiology unit of JRRH follows up ~200 children with different cardiopathies. The unit has 1 paediatric cardiologist, 1 medical officer, and 4 nurses. Ethical clearance for the present study was obtained from the Research Ethics Committee of Kampala International University Western Campus and (ref. no. KIU-2022-163). Administrative clearance to conduct the study at JRRH was obtained from the hospital executive director. Written informed consent for all study participants was obtained from the primary caregiver.

Study population

We studied all children from 6 months to 12 years with CHD in the paediatric cardiology clinic during the study period. Children who

had received blood transfusion(s) within the last 3 months, those with corrected CHD, and those who had chronic diseases, e.g. chronic renal and liver diseases, as well as leukaemia, were excluded from the study.

Sample size

A total of 140 children with CHD were recruited to participate in the study. This was based on the Fleiss formula of a sample size of 2 proportions, maintaining a 95% level of confidence, 80% power, and prevalence of iron deficiency of 41.6% among children with CHD compared with 13.3% among the controls.[10] Participants were consecutively enrolled in the study until the required sample size was achieved.

Study procedure

Study participants were recruited through the clinic register. Participants were given study information and then consented to the study. A pulse oximeter was used to measure oxygen saturation. Body weight and height/length were determined for all participants. To minimise variability in sample collection and analysis, a standardised protocol was used for sample collection, storage and analysis. A senior phlebotomist was used to collect 4 mL of venous blood into an ethylenediamine tetra-acetic acid (EDTA) tube from each study participant through an aseptic technique. He then transferred the samples to the main laboratory of JRRH for analysis, where the samples were analysed within 30 min of collection and results were checked by the principal investigator. Complete blood count was analysed using Sysmex Automated Hematology Analyzer (Sysmex, Japan). Serum ferritin was analysed using a Cobas –e411 Analyzer (Roche Diagnostics, Switzerland). A structured questionnaire (translated from English to the most common local language) was used to collect data.

Data management and analysis

Completed questionnaires were entered into a computer using EpiData (version 4.1; EpiData Association, Denmark). The data were exported to STATA 17.0 (StataCorp., USA) for analysis. IDA was defined as a serum ferritin level <15 µg/L, while Hb levels were defined as recommended by the World Health Organization (WHO) for children as follows: 6 months to <5 years, Hb <11 g/dL; 5 to <12 years, Hb <11.5 g/dL; and 12 to <15 years, Hb <12 g/dL.[11] The WHO charts for weight-for-age for children under 5 years and BMI-for-age for children 5 to 19 years were used to categorise weight. Stunting was categorised using the WHO length-/height-for-age charts. The prevalence of iron deficiency was calculated as a fraction of children with CHD who had IDA. It was expressed as a percentage with a corresponding 95% confidence interval (CI). For factors associated with IDA among children with CHD, logistic regression analysis was used in both bivariate and multivariate analysis. All factors with *p*-values <0.2 were moved to multivariable analysis. A variable with $p<0.05$ at multivariate analysis was considered statistically significant.

Results

Patient characteristics

The majority (80%) of the children were over 12 months old and over half (56.4%) were male. Over two-thirds of the children had acyanotic CHD. Only 20.3% of the children were on iron supplementation and over 70% reportedly weekly consumption of red meat. Only 32 (22.9%) of the children had serum ferritin <15 µg/L (Table 1).

Characteristics of caregivers of children with CHD

The majority (59.3%) of the caregivers were older than 30 years, and most (59.3%) were unemployed (supplementary Table 1;http://coding.samedical.org/file/2357).

Red blood cell indices of children with CHD

The average Hb, mean corpuscular Hb (MCH), RDW, and RBC was higher among patients with cyanotic compared with those with acyanotic heart disease while MCV and MCHC were higher among patients with acyanotic heart lesions. This is illustrated in Supplementary Table 2 (http://coding.samedical.org/file/2357).

Types of CHDs among study participants

Of the 140 participants in the study, 29 (20.7%) had isolated VSD and another 15% had an isolated ASD (supplementary Fig. 1; http://coding.samedical.org/file/2357).

Prevalence of IDA among children with CHD

Twenty-nine (20.7%) out of the 140 children with CHD had serum ferritin levels <15 µg/dL and Hb levels <11.5 g/dL. The prevalence of IDA was 20.7% (95% CI 14.7 - 28.3).

Of the 29 children with IDA, the majority (68.9%) had acyanotic CHD. Nine out of 34 children with cyanotic CHD had IDA while 20 out of 106 children with acyanotic CHD had IDA. Children with cyanotic CHD were more likely to have IDA.

Bivariate analysis of patient factors associated with iron-deficiency anaemia

Among the patient factors, patients' age, iron supplementation and being stunted were associated with IDA ($p<0.2$) (Table 2).

Table 1. Characteristics of children with CHD (*N*=140)

Variable	Frequency, *n* (%)
Age (months)	
≤12	28 (20.0)
Gender	
Female	61(43.6)
CHD type	
Acyanotic	106 (75.7)
Cyanotic	34 (24.3)
Oxygen saturation (%)	
<90	22 (15.7)
≥90	118 (84.3)
Iron supplementation	
No	99 (70.7)
Weekly red meat consumption	
No	40 (28.6)
Hb (g/dL)	
≤11.5	76 (54.3)
>11.5	64 (45.7)
Serum ferritin (µg/dL)	
<15	32 (22.9)
≥15	108 (77.1)
Dewormed in last 6 months	
No	79 (56.4)
Yes	61 (43.6)
Underweight	
No	83 (59.3)
Yes	57 (40.7)
Stunted	
No	73 (52.1)
Yes	67 (47.9)

CHD = congenital heart disease; Hb = haemoglobin.

Table 2. Bivariate analysis of patient factors associated with IDA

Variable	IDA		cOR (95% CI)	*p*-value
	Yes	No		
Age (months)				
≤12	10 (34.5)	18 (16.2)	1.00	
>12	19 (65.5)	93 (83.8)	0.37 (0.15 - 0.92)	0.03
Gender				
Female	15 (51.7)	46 (41.4)	1.00	
Male	14 (48.3)	65 (58.6)	0.66 (0.29 - 1.50)	0.32
CHD type				
Acyanotic	20 (69.0)	86 (77.5)	1.00	
Cyanotic	9 (31.0)	25 (22.5)	1.55 (0.63-3.82)	0.34
Oxygen saturation				
<90	6 (20.7)	16 (14.4)	1.00	
≥90	23 (79.3)	95 (85.6)	0.65 (0.23 - 1.83)	0.41
Iron supplementation				
No	27 (93.1)	72 (64.9)	1.00	
Yes	2 (6.9)	39 (35.1)	0.14 (0.03 - 0.61)	0.01
Weekly red meat consumption				
No	12 (42.9)	28 (25.0)	1.00	
Yes	16 (57.1)	84 (75.0)	0.44 (0.19 - 1.05)	0.07
Dewormed in last 6 months				
No	16 (57.1)	63 (56.3)	1.00	
Yes	12 (42.9)	49 (43.7)	0.96 (0.42 - 2.22)	0.93
Underweight				
No	19 (65.5)	64 (57.7)	1.00	
Yes	10 (34.5)	47 (42.3)	0.72 (0.31 - 1.68)	0.44
Stunted				
No	11 (37.9)	62 (55.9)	1.00	
Yes	18 (62.1)	49 (44.1)	2.07 (0.89 - 4.79)	0.09

IDA= iron-deficiency anaemia; cOR = crude odds ratio; CI = confidence interval.

Table 3. Multivariate analysis of factors associated with IDA

Variable	cOR	aOR	95% CI	*p*-value
Iron supplementation				
No	1.00	1.00		
Yes	0.14	0.14	0.03 - 0.68	0.01
Age (months)				
≤12	1.00	1.00		
>12	0.37	0.40	0.15 - 1.07	0.07
Stunted				
No	1.00			
Yes	2.07	2.21	0.89 - 5.48	0.09

IDA = iron-deficiency anaemia; cOR = crude odds ratio; aOR = adjusted odds ratio; CI = confidence interval.

Bivariate analysis of caregiver factors associated with IDA

Only caregiver age was associated with the presence of IDA (supplementary Table 3; insert URL here).

Factors associated with IDA

Lack of iron supplementation was the only factor to be significantly associated with IDA among children with CHD (Table 3).

Discussion

The overall prevalence of IDA in the present study was 20.7%. When categorised by type of CHD, the prevalence of IDA was 26.5% and 18.9% among children with cyanotic and acyanotic CHDs, respectively. A study in Tanzania reported the prevalence of IDA among children with CHD to be 20.2%,[12] which was similar to findings in the present study. Another study in India reported the prevalence of IDA among children with cyanotic CHD to be

40.7%[9] – the observed difference may be attributed to the lower Hb levels used to define anaemia in the present study. Patients with CHD are known to have paradoxically higher Hb levels even in the presence of anaemia. Overall the prevalence of IDA among Ugandan children was reported to be 21.1%.[13] However, the present study was conducted among children 0 to 8 years old in an urban setting, and in another study, the prevalence of IDA was reported to be 41.5%.[14] The present study included children aged 6 - 23 months and a Mentzer index >13 was suggestive of the presence of IDA.

Although other red blood cell indices were relatively similar between acyanotic and cyanotic heart disease patients, the red blood cell count in cyanotic patients was more than twice the value of acyanotic patients. This is because tissue hypoxia increases erythropoietin production and this causes the release of immature erythrocytes. [15]

Lack of iron supplementation was significantly associated with IDA in our study. Less frequent consumption of red meat, a rich source of iron, was reported to be a significant factor associated with IDA.[12] In our study, meat consumption was not associated with IDA. Iron deficiency is the most common micronutrient deficiency and is almost always deficient among children with malnutrition. A study in India[16] reported malnutrition to be more common in children with CHD compared with participants in the control group. Children with CHD experience chronic malnutrition and in the present study more than 40% of the participants were underweight, while nearly half (47.9%) were stunted. However, both stunting and underweight were not associated with IDA in this study.

Study limitations

Similar Hb levels were used to define anaemia in both children with cyanotic and acyanotic CHD. This may have led to an underestimation of the prevalence of IDA in patients with cyanotic heart disease.

Conclusion and recommendations

The prevalence of IDA among children with CHD was high and it was associated with a lack of iron supplementation. Children with CHD should be routinely screened for iron status and supplemented whenever indicated.

Declaration. None.

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Conflicts of interest. None.

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