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PREVALENCE OF IRON DEFICIENCY IN CHILDREN WITH CYANOTIC HEART DISEASE SEEN AT KENYATTA NATIONAL HOSPITAL AND MATER HOSPITAL NAIROBI
M. O. Lang'o, MBChB, MMed (Paed), Paediatrician, Gertrude's Children's Hospital, P. O. Box 42325 - 00100, Nairobi, Kenya, J. N. Githang'a, MBChB, MMed (Path), Senior Lecturer, Department of Pathology and C. A. Yuko-Jowi, MBChB, MMed (Paed), Senior Lecturer, Department of Paediatrics and Child Health, College of Health Sciences, University of Nairobi, P. O. Box 19676 -00202, Nairobi, Kenya

Request for reprints to: Dr. M. O. Lang'o, Gertrude's Children's Hospital, P. O. Box 42325 - 00100, Nairobi, Kenya

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M. O. LANG'O, J. N. GITHANG'A and C. A. YUKO-JOWI

ABSTRACT

Objective: **To establish the prevalence of iron deficiency among children with cyanotic heart disease.**
Design: **Cross-sectional study.**
Setting: **The study was carried out at Kenyatta National Hospital and Mater Hospital from August to December of 2007. A total of 112 children meeting the eligibility criteria were recruited from the wards and the cardiac clinics.**
Subjects: **These were children less than 18 years of age, with cyanotic heart disease confirmed on ECHO, presenting at the paediatric cardiac clinic of the two hospitals or admitted in the wards at Kenyatta National Hospital. These were patients who had not undergone surgical correction.**
Results: **The prevalence of iron deficiency was found to be 16.9% (95% CI 9.8-24.1%).**
Conclusion: **There is a high prevalence of iron deficiency among patients with congenital heart disease with cyanosis in the two institutions. Routine screening for iron deficiency is recommended for these children and those found to be deficient should be treated.**

INTRODUCTION

Uncorrected congenital cyanotic heart lesions (and some acyanotic lesions which later have reversal of blood flow from right to left with the development of Eisenmenger's complex) keep the body in a state of constant hypoxia. This hypoxia triggers a physiological increase in erythropoietin release leading to stimulation of the bone marrow to produce more red cells in an effort to increase the body's oxygen carrying capacity, so as to improve oxygen delivery to the tissues. With persisting right to left shunt, the arterial oxygen tensions remain perpetually low and so the production of more and more red cells goes unabated leading to polycythemia. This seemingly noble physiological response eventually leads to depletion of iron stores.

In these patients, the total haemoglobin is normal, high or slightly reduced compared to aged-matched normal individuals without cyanosis. However, the MCV, MCH and serum ferritin are usually comparatively lower than their peers as shown by Cemile *et al* (1) - a phenomenon known as relative anaemia. Irrespective of cause, iron deficiency leads to a significant increase in whole blood viscosity in erythrocytotic patients, and the viscous effect rises with decreasing erythrocyte mean corpuscular haemoglobin (2).

Patients with iron deficiency will have higher morbidity rates presenting with symptoms of hyperviscosity such as cerebrovascular accidents, cyanotic spells, anorexia, exercise intolerance, poor appetite, poor weight gain, irritability and poor mental development. Treatment of iron deficiency has been shown to reverse all these symptoms. Gaiha *et al* (3) showed that hyperviscosity symptoms occurred at a lower PCV level (0.52-0.58) among cyanotic patients with iron deficiency as compared to those who were iron sufficient where symptoms occurred at the mean PCV of 0.68. Among the iron deficient group, hyper cyanotic symptoms were relieved with iron supplements, and this symptomatic relief was accompanied by an average haemoglobin rise of 2.1g/dl (3). Similar effects were demonstrated by Perfloff *et al* (4).

MATERIALS AND METHODS

Study population: These were children less than 18 years of age with ECHO confirmed cyanotic heart disease who had not undergone corrective surgery, presenting at the paediatric cardiac clinic of Kenyatta and Mater Hospitals or admitted in the wards at Kenyatta National Hospital. Those already on iron supplements were excluded from the study.

Sample size calculation: The sample size was calculated using Fischer's method.

Sampling: Patients meeting the eligibility criteria were consecutively recruited from the two hospitals between 8 and 3 pm, till the desired sample size was attained.

Study duration: This study was carried out over five months (August 2007 to December 2007).

Study design: This was a cross-sectional study.

Procedures: Patients were identified and recruited into the study once consent was obtained. Body temperature was taken; height and length were measured in centimeters using a stadiometer. Weight was taken using a step-on weighing scale, or an infant weighing scale for infants. Date of birth, sex and residence was recorded on the questionnaire. A history and physical examination was used to help exclude inflammatory disease which are known to affect ferritin levels.

About 2ml of venous blood was drawn using a 5cc syringe and divided equally into a plain bottle and EDTA bottle. The complete blood count was done using the electronic cell counter – Cell-Dyn 1300. Ferritin levels were performed using a semi automated process using Humalyzer 2000.

Study definitions

(i) *Iron deficiency:* Depletion of the body's iron stores as evidenced by low ferritin levels that are below the lower limit of the age specific reference range (5). In this study, ferritin was the gold standard for measuring iron stores.

(ii) Low MCV and low MCH was defined as an MCV or MCH values that is below the lower limit of the age specific reference range.

Data analysis: The study population was described in terms of their demographic and clinical characteristics using means, medians and proportions. Prevalence of iron deficiency was calculated as proportion of children with ferritin values below -2SD of the reference mean. Children with iron deficiency were compared to those without to determine associated factors. Chi-square tests and t-test were used to determine factors with significant associations. Data was analysed using the Statistical Package for Social Sciences software (SSPS).

Ethical considerations: The hospitals' ethics committees approved the study. Written consent was obtained from guardians for each participant after detailed explanation.

RESULTS

One hundred and twelve children were recruited into the study. Their ages ranged from one month to 17 years, with a median age of four years and five months. The mean age was 5 years 10 months. Males were 59 while 53 were female, giving a male to female ratio of 1:1. The commonest heart lesion encountered was Tetralogy of Fallot (54%).

Fifty nine out of 112 patients (52.6%) were below five years of age, while 53 out of 112 (47.3%) were older than five years. The nutritional status was analysed based on the CDC 2000 guidelines. Twenty (17.9%) were classified as moderately stunted, while 25 (22.3%) were severely stunted. Moderate wasting was seen in 17 (15.2%) of the study population while 23 (20.5%) were severely wasted (Table 1).

Heart lesions were divided into those with predominantly left to right shunt and those with predominantly right to left shunt. Complex lesions seen in this study included dextrocardia and a host of other complicated cardiac anatomy lesions. The most frequently encountered heart lesion was Tetralogy of Fallot followed by tricuspid atresia (Table 2).

Table 1
Summary of the characteristics of the study population (n=112)

Parameter	Category	No.	(%)
Age (years)	<1	20	17.8
	>1 – 5	39	34.8
	>5 – 12	35	31.3
	> 12	18	16.1
Sex	Male	59	52
	Female	53	48
Nutritional status	Normal and mild stunting	67	59.8
	Moderately stunted	20	17.9
	Severely stunted	25	22.3
	Normal and mild wasting	72	64.3
	Moderate wasting	17	15.2
	Severe wasting	23	20.5

Table 2
Frequency of encountered heart lesions (n=112)

Lesion	No.	(%)
Predominantly right to left shunt		
Tetralogy of fallot	61	54
Tricuspid atresia	9	8
Pulmonary atresia with VSD	6	5.3
Double outlet right ventricle	4	3.5
Critical pulmonary stenosis	3	2.6
Predominantly left to right shunt		
Truncus arteriosus	2	1.7
Transposition of great arteries	5	4.4
Eisenmengers and other complex heart lesions	22	19

Eighteen out of 106 patients had ferritin levels below the lower limit of their age specific reference ranges giving an iron deficiency prevalence of 16.9% (CI 9.8-24.1%). Half the study population had MCV and MCH values below the age specific reference ranges (50.5% for low MCV and 50% for low MCH). Findings of microcytic hypochromic cells were seen in 33 out of 106 patients giving a prevalence of 31.1% (Table 3).

There was no statistically significant difference in the occurrence of any of the haematological derangements between the predominantly left to right shunting lesions and the predominantly right to left shunting lesions (Table 4).

Table 3
Summary of the haematological parameters

Parameter	Mean (95% CI)	Median	Inter- Quartile range	Normal and acceptable values		Derangements of interest	
				No.	(%)	No.	(%)
Serum ferritin	48.9 (40.5-57.3)	39	61.25	88/106	83.1	18/106	16.9
MCV	76.3 (74.2-78.4)	77	17	51/103	49.5	52/103	50.5
MCH	25.8 (24.9-26.8)	25.45	7.17	51/102	50	51/102	50
Hypochromic microcytic cells				73/106	68.9	33/106	31.1

In this study all iron deficient patients fell in the group of children aged less than five years of age. This was statistically significant (p= 0.000). The other significant factor associated with iron deficiency was stunting, specifically, severe stunting. There was a five fold increased likelihood of having iron deficiency with the presence of severe stunting (odds ratio 4.88 [95% CI 1.48-16.2], p = 0.005). No statistically significant relationship was noted between iron deficiency and sex (p=0.301) and between iron deficiency and wasting (p=0.673) (Table 5).

DISCUSSION

The overall prevalence of iron deficiency in this study was 16.9%, which is almost similar to what was found in the study done in India by Gaiha *et al* (3) where they reported a prevalence of 18.2% and much higher than the prevalence of 7% reported by Murila *et al* (6) in Kenya who looked at a generally healthy population of children less than 5 years of age. Interestingly, in our study all the 18 patients found to be iron deficient were below five years of

Table 4
Influence of the type of heart lesion on the haematological derangements

Parameter	CCHD predominantly Left to right shunt No. (%)	CCHD predominantly Right to left shunt No. (%)	OR (95% CI) No. (%)	P-value
Serum ferritin				
Iron deficiency	12/70 14.6	2/5 28.6	0.43 0.06-3.63	0.302
Rbc indicators				
Low MCV	36/82 43.9	2/7 28.6	1.96 0.31-15.57	0.690
Low MCH	22/82 26.8	1/7 14.3	2.20 0.24-51.26	0.690
PBF-Microcytic hypochromic cells	28/82 43.1	1/7 14.3	3.11 0.34-71.99	0.420

Table 5
Non-cardiac correlates of iron deficiency

Parameter No. (%)	Iron deficiency No. (%)	No iron deficiency	OR	95% CI	P-value
Age					
<60 months	18/18 100	41/94 43.6	-	-	0.000
≥ 60 months	0/18 0	53/94 56.4			
Sex					
Male	11/18 61.1	48/94 51	1.5	0.49-4.76	0.301
Female	7/18 38.9	46/94 49			
Nutrition status stunting					
Severe	9/18 50	16/94 17	4.88	1.48-16.2	0.005
Moderate	1/18 5.5	19/94 20.2	0.22	0.01-1.85	0.19
Mild to normal	8/18 44.5	59/94 62.8	0.47	0.15-1.46	0.23
Wasting					
Severe	5/18 27.8	32/93 34.4	0.73	0.21-2.48	0.78
Moderate	6/18 33.3	22/93 23.6	1.61	0.47-5.38	0.386
Mild to normal	7/18 38.9	39/93 42.0	0.88	0.28-2.75	0.98

age. Drossos *et al* (7) from Italy in 1981 examining a total of 38 cyanotic heart disease children, found an iron deficiency prevalence of 12.5% in children 6 to 12 years of age. Similarly, in the same study, children less than five years still contributed the bulk of the iron deficiency group with a prevalence of 37.5%.

Ferritin measurements as indicator of iron status are prone to giving false negative results as they are affected by many factors causing inflammation including infection. This leads to a falsely elevated ferritin level, thus the false negatives. In our local set up, with high prevalence of infectious diseases, it is possible that our ferritin assays could have underestimated the prevalence of iron depletion.

From this study, we found that 40.1% (45 out of 112) children were stunted. This is much higher than the national figure of 30% reported in the Kenya Demographic and Health Survey (KHDS) 2003. Out of these, 22.3% were severely stunted while 17.9% were classified as moderately stunted. Wasting was seen in 35.7% (40 out of 112) of our study population, a figure much higher than the national figure of 6% reported in the KHDS 2003. Severe wasting was seen in 20.5% of the study population while moderate wasting was seen in 15.2%. This was however an expected finding given the burden of the heart disease on its own is expected to interfere with growth and general well being and food intake.

In conclusion, there is a high prevalence of 16.9% of iron deficiency in children with cyanotic heart disease attending the cardiac clinics at Kenyatta National Hospital and Mater Hospital.

We recomend that, children with cyanotic heart disease should routinely be screened for iron deficiency, using a combination of blood picture and ferritin levels and those found deficient should be treated accordingly.

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