

Original Research Article

Prevalence, profile of malnutrition and iron deficiency anemia in children with cyanotic congenital heart defects: a case control observational study in a tertiary care hospital in North India

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ABSTRACT

Background: Children with congenital heart disease (CHD) are prone to malnutrition. Children with cyanotic CHD [CCHD] are specifically affected due to chronic hypoxia and iron deficiency anemia which is overlooked by pediatrician. This can have a significant effect on the outcome of surgery. Our objective was to determine the burden and determinant of malnutrition in children with several types of cyanotic congenital heart disease (CCHD).

Methods: This case-control study included 80 children with symptomatic CCHD, and 40 healthy children matched for age and sex as a control group. Clinical evaluation and laboratory assessment of nutritional status were documented. Anthropometric measurements were recorded and Z scores for weight for age (WAZ), weight for height (WHZ), and height for age (HAZ) have been calculated. Haemoglobin, red cell indices and serum iron, total iron binding capacity and serum ferritin was done in cases and controls.

Results: The overall prevalence of malnutrition was 72.5% in patients with CCHD and 22.5% in controls. Severe malnutrition was diagnosed in 68.9% of cases. All anthropometric measurements which markers of nutritional state are were significantly lower in the patients group compared to controls. The prevalence of iron deficiency anemia (IDA) was 47.5% in the study population. The study also showed that hemoglobin and hematocrit levels, RBC count were paradoxically higher in the cyanotic CHD as compared to the healthy controls though the iron studies revealed the iron deficiency. The mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH) mean corpuscular hemoglobin concentration (MCHC), serum ferritin, serum iron, total iron binding capacity (TIBC), values were the parameters, which were found to be statistically significant to differentiate the study groups.

Conclusions: Malnutrition is a very common problem in children with symptomatic CCHD, the prevalence of IDA in children with CCHD was found to be high.

Keywords: Anemia, Cyanotic congenital heart disease, Iron deficiency, Malnutrition

INTRODUCTION

Children with congenital heart diseases (CHD) have been documented to have poor nutritional status. Factors responsible for this include genetic predisposition, pre-natal factors, increased metabolic demands in the

presence of heart failure, poor oxygenation and reduced availability, intake and absorption of nutrients.¹ Malnutrition is a major burden amongst children in developing countries due to prevailing food insecurity, poverty, large family size, ignorance and rampant preventable infectious diseases.² Thus, children with

CHD from resource poor countries may be at higher risk of severe malnutrition by virtue of their exposure to above factors that predispose to malnutrition.³

Children with cyanotic CHD in addition to macronutrient deficiency suffer from micronutrient deficiency especially iron deficiency. 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. In these patients, the total hemoglobin 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 Onur CB et al, a phenomenon known as relative anemia.⁴

Patients with iron deficiency will have higher morbidity rates presenting with symptoms of hyper viscosity 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 M et al, showed that hyper viscosity 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 0.68.⁵ Among the iron deficient group, hyper cyanotic symptoms were relieved with iron supplements, and this symptomatic relief was accompanied by an average hemoglobin rise of 2.1g/dl.⁵ Similar effects were demonstrated by Perloff JK et al.⁶

It is important to mention that pediatric cardiac programs are not fully established in our part of world like in many developing countries subsequently author have lot of children with unoperated congenital heart defect. The epidemiological data on CHD related malnutrition and associated micronutrient deficiency is lacking. Therefore, this study aimed to assess the prevalence, patterns, of malnutrition in Kashmiri children with cyanotic CHD. Furthermore, in this study author aimed to access the iron status in children with CCHD.

METHODS

This was a case-control study of 80 children with diverse, symptomatic cyanotic CHD, admitted in tertiary care pediatric hospital of GMC Srinagar from Jan 2016 to Jan 2018. Eighty age-and sex-matched apparently healthy controls without CHD who attended same hospital on OPD basis for minor ailment. Informed consent was obtained from parents and other caregivers before enrolment. CHD was diagnosed or excluded by clinical,

echocardiographic and other routine tests. Cases and controls were frequency matched for age and sex, the two critical demographic variables that could influence the outcome of interest, that is, malnutrition

Anthropometric measurements included weight (kilogram), length (centimeter). Z scores for weight for age (WAZ), weight for height (WHZ), and height for age (HAZ) was computed using WHO global database.^{7,8}

The WHO recommends the use of standard definitions and classifications for malnutrition based on calculated Z scores for anthropometric indices.^{7,8}

The WHO global database on child growth and malnutrition recommends a cut-off Z score of ≤ 2 to classify low WAZ (underweight), low HAZ (stunting) and low WHZ (wasting) as moderate malnutrition, and a Z score of ≤ 3 SD to define severe malnutrition. Normal nutrition is indicated by a WAZ Z score of between ≥ 2 and ≤ 2 .

Hemogram was done using Sys Mex CBC analyzer. Serum iron, ferritin and TIBC (total iron binding capacity) were done using siemens fully computerized biochemistry analyzer. Serum ferritin was used as gold standard for defining iron deficient states using cutoff level of serum ferritin as per WHO recommendation.⁹

Echocardiography was performed using the Seimens Accuson S2000 multipurpose system with different probe sizes.

Statistical analysis

Data were analyzed using the statistical package for social sciences (SPSS) release 16. Data with a normal distribution are presented as mean and SD. The mean of two groups was compared by t-test. Non-parametric values were represented as median and range, and the medians of two groups were compared by Mann-Whitney U test. Qualitative data were represented by their frequency and relative percentage, and chi-square test was used for testing association of qualitative data. A p-value of <0.05 was considered statistically significant.

RESULTS

Table 1 gives baseline characteristic of study population compromising cases and controls. The main study groups (cases and controls) were comparable regarding age, sex and another baseline characteristic. Overall n=6 (5%) were aged 0 to 6 months, n=4 (10%) were aged 6 months to 1 year, n=20 (50%) were between 1 year to 5 year and n=10 (25%) were between 5 to 10 year. There were no significant differences between patients and controls regarding the demographic characteristic i.e. age, sex. The anthropometric measurements height and weight were significantly low in cases than in controls.

The most common cyanotic CHD was tetralogy of Fallot, followed by Eisenmengers syndrome due to uncorrected ventricular septal defect (VSD) and patent ductus arteriosus (PDA). Table 3 shows the prevalence and types of malnutrition observed in the main study groups. 29 (72.5%) of 40 children with CHD were malnourished as compared to 9 (22.5%) children without CHD. In

children with CHD, prevalence of wasting (low WHZ), underweight (WAZ), stunting (low HAZ) were significantly higher compared with the control group. Also, the relative proportion of children with severe malnutrition was significantly higher in patients with CHD.

Table 1: Baseline characteristic of study population.

Variable	Controls n=40	Cases n=40	P value
Age range Months	1.5-120	1.5-120	
Sex ratio			
Male	1.3:1	1.2:1	
Female			
Height or length(cm) median /range	84.9/50-140	72/50-119	0.02
Weight (kg) median /range	11.3/4-25	7.1/3.4-19	0.001

Table 2 Distribution of cardiovascular malformations in affected children (n=40).

Tetralogy of Fallot	16 (40%)
Transposition of great arteries (TGA)+VSD with PS	3 (7.5%)
Transposition of great arteries (TGA)+VSD without PS	2 (5%)
Congenitally corrected transposition +VSD+PS	2 (5%)
Pulmonary atresia with VSD	3 (7.5%)
Single ventricle with PS (pulmonary stenosis)	2 (5%)
Single ventricle without PS	3 (7.5%)
Supra cardiac TAPVC; total anomalous pulmonary venous connection	2 (5%)
DORV (double outlet right ventricle) +VSD+PS	2 (5%)
Truncus arteriosus	1 (2.5%)
Eisenmenger syndrome	4 (10%)

Table 3: Nutritional status in cases and controls.

Nutritional status	Controls n=40	Cases n=40	P value
Normal	31(77.5%)	11(27.5%)	<0.05
Malnutrition	9 (22.5%)	29 (72.5%)	
Pattern of malnutrition			
Underweight (WAZ)	4 (44.4%)	9 (31.0%)	0.001
Wasting or acute malnutrition (WHZ)	3 (33.3%)	6 (20.65%)	0.001
Stunting or chronic malnutrition (HAZ)	2 (22.2%)	14 (48%)	0.001
Degree of malnutrition			
Moderate malnutrition	8 (88.8%)	9 (31.0%)	0.78
Severe malnutrition (z score<-3)	1 (11.1%)	20 (68.9%)	0.001

Table 4: Body iron stores.

Iron deficient state	Cases	Controls
Yes	19 (47.5%)	10 (25%)
No	21 (52.5%)	30 (75%)

Table 4 depicts the body iron stores in cases and controls. In this study, ferritin was the gold standard for measuring iron stores. 47.5% n=19 children with cyanotic CHD were

iron deficient state as compared to 25% n=10 in healthy children.

DISCUSSION

Different types of cardiac malformation can affect nutrition and growth to varying degrees. The severity of malnutrition can range from mild under-nutrition to failure to thrive.¹⁰ Present study has been performed to evaluate growth and nutritional status with specific focus

on iron deficiency anemia of children with cyanotic CHD.

The high prevalence of 72.5% in our CHD group demonstrates the importance of malnutrition in patients with CHD. Moreover, 68.9% of cases had severe malnutrition. Previous reports showed that CHD-related malnutrition is particularly common in developing countries, but prevalence varies widely from 27% up to 90.4%. For instance, Turkey, Mehrizi A et al, and Drash A et al, reported a malnutrition prevalence of 27% in children with CHD, whereas a more recent Turkish study described a prevalence of 85%.^{11,12} In South India, Vaidyanathan B et al, and his colleagues reported a high

prevalence of underweight (59.0%) in children with CHD.¹³ In Nigeria, Okoromah CA et al, and his colleagues conducted a case-control observational study to evaluate prevalence and predictors of malnutrition in children with uncorrected symptomatic CHD describing a prevalence of 90.4%.¹⁴ The high prevalence of malnutrition in present study may be explained by several factors including the distribution pattern of cardiac lesions, the presence of severe complications of CHD, such as CHF, and the prolonged absence of surgical CHD correction. This study was conducted in the tertiary teaching hospital in our state to which cases with severe CHD and its complications are likely to be referred to for evaluation and management.

Table 5: Blood parameters.

Blood parameter	Cases n=40	Controls n=40	P value
Haemoglobin (gm/dl) Mean \pm SD	14 \pm 2.7	10.6 \pm 1.34	0.002
RBC count 10 ⁵ /microlit Mean \pm SD	5.34 \pm 1.48	3.5 \pm 0.5	0.01
Haematocrit (%) Mean \pm SD	48.3 \pm 5.7	34.9 \pm 3.07	0.02
MCV (fl) Mean \pm SD	69.9 \pm 5	81.07 \pm 7.19	0.02
MCH (pg) Mean \pm SD	22.31 \pm 3	30 \pm 3.16	0.001
MCHC (gm/dl Mean \pm SD	25.5 \pm 2.7	30.14 \pm 2.26	0.001
TIBC microgm/dl Median (range)	415 (143-775)	380 (172-816)	0.0008
Serum iron microgm/dl Median (range)	50 (10-161)	64 (19-160)	0.001
Serum ferritin nanogm/dl Median (range)	12 (10-56)	30 (10-82)	0.018

The relative proportions of underweight, wasting and stunting in the patient group were 31%, 28%, and 60%, respectively. Okoromah CA et al, and his colleagues reported that the relative proportions of underweight, stunting, and wasting, were 20.5, 28.8, and 41.1%, respectively.¹⁴ Ratanachu S et al, and Pongdara A et al, study found that relative proportions of underweight, stunting, and wasting in Thailand children with CHD were 28,16 and 22%, respectively.¹⁵ Stunting rather than wasting was found to be the most common type of malnutrition in present study. This is in contrast to the results reported by Okoromah CA et al, and also the preponderance of underweight described in the study of Ratanachu S et al, and Pongdara A et al.^{14,15} These difference in pattern of malnutrition can be due to prolonged hypoxia in children with cyanotic CHD which lead to chronic growth failure and hence stunting. Also due to lack of pediatrics cardiac surgeries in our area there are lot of children with unoperated CHD, making them susceptible for chronic malnutrition and stunting, furthermore regional variations in the distribution of malnutrition may also contribute to these differences. Finally, and this may be the most important aspect, previous studies differed from present study concerning their design, characteristics of the study populations, and reference growth standards used for classification of malnutrition.

The most common cyanotic CHD in present study was tetralogy of Fallot, followed by uncorrected congenital acyanotic heart lesions which later have reversal of blood flow from right to left with the development of Eisenmenger's complex.

The prevalence of iron deficiency anemia based on serum ferritin levels which were lower than reference range for age was 47.5% n=19 in patients with CCHD, whereas it was only 25 % n=10 in controls. There is a paucity of literature discussing iron deficiency among children with CCHD and these studies have shown varying results. Our result is similar to prevalence rate found by Mukherjee S et al.¹⁶ In 1990, West et al, have demonstrated that more than one-third of patients with CCHD had iron deficiency.¹⁷ In another study done by Olcay L et al, the prevalence of IDA was found to be 52.2%.¹⁸ In a study done in India by Gaiha M et al, a prevalence of 18.18% was reported, however the subjects of this study were adolescents and young adults.⁵

The mean hemoglobin, hematocrit and RBC count was significantly high in cases than in controls. Marked hypoxemia in these children is potent stimulator of erythropoiesis.^{17,19} Iron deficiency is reported to be common in individuals with CCHD even in the presence of high hematocrit levels.²⁰⁻²² These groups of children are often assumed not to be iron deficient because of

elevated red cell mass. There was statistical difference in MCV, MCH, MCHC among case and controls. The use of simple red cell indices has been shown to be effective in identifying iron deficiency in individuals suspected to be deficient in iron.⁴

In the study conducted by Mukerjee S et al, the frequency of cyanotic spells in the iron deficient group was 25% and association between iron deficiency anemia and cyanotic spells were found to be statistically significant (p value-0.042).¹⁶ Children with IDA had eight times the risk of having cyanotic spells compared to the children who were not iron deficient highlighting the need of iron supplementation in children with cyanotic CHD

Limitations of this study were based on the present study is limited by a small sample size. Therefore, it may not be adequately powered to draw major statistical conclusions. In addition, it was carried out at a single tertiary care center, and hence likely to have a referral bias. Another issue is the study population which also includes children younger than 6 months, which make the mean values of the hematological parameters on the higher side.

CONCLUSION

Conclusion There is high rate of malnutrition in children with CCHD, with stunting more common suggesting chronic malnutrition in these children. Furthermore, these children are also susceptible to iron deficiency anemia and have low body iron stores. The ferritin levels in children with cyanotic congenital heart disease showed little correlation with the hemoglobin levels. Present study highlights the need for proper nutritional rehabilitation in these children with special attention to iron supplementation as low iron level increases morbidity in these children.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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