Al-Nahrain University
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Anemia in patients with congenital heart diseases

Research submitted to department of pediatric /college of medicine/

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By

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LIST OF TABLES &FIGURES

DEDICATION

To my supervisor and teacher Dr.Sinan

Abd al-razzaq Ibraheem

To anyone who has shown me friendship and kindness during my field travel.

And to my kind and wonderful teachers & mentors who took the time and effort to teach and serve as 3role models. I am so grateful for your support, compassion, encouragement and unselfishness; .

ABSTRACT

Background:decreased concentration of hemoglobin and RBC′s mass compared with that in age matched controls.

The decrease may result from blood loss, increased destruction of RBCs (hemolysis), or decreased production of RBCs.

Anemia is common in all children with congenital heart disease , especially in children with signs of heart failure .

AIM: To determine the incidence of anemia in children with CCHD by noninvasive , inexpensive, and easy laboratory methods,

patients and Methods :This was a prospective study conducted from 15th of November 2018 to 7th of January 2019 At Al-Imamain Al-Kadhimain medical city. The study included 60 neonate patients who admitted to the pediatric ward.

Results: The study sample included 60 patients presented with congenital heart disease .(55%) of the patients were males and (45%) were females.The Majority of patients (48.33%) were above 1 year age .48.33% of male, and 35% of female patients are anemic.

Conclusions : Anemia is not uncommon in CHD patients attending hospital and is associated with a 3-fold increased risk of death. Screening for anemia should be part of the routine assessment of CHD patients for risk stratification and treatment when correctable causes are identified.

INTRODUCTION

Anemia is Decreased concentration of hemoglobin and RBCs mass compared with that in Age-matched controls.(1)

Table- 1 :Normal values of Hb for age(1)

Age	Hb/dl		Haematocrit%	
Cord blood	16.8	13.7-20	55	45-65
2 weeks	16.5	13-20	50	42-66
3 months	12	9.5-14.5	36	31-41
6m-6y	12	10.5-14	37	33-42
7-12y	13	11-16	38	34-40

Classification of anemia according to MCV (morphological)(2)

- Low (<75 fl) Microcytic anemia
- Normal (75-90 fl) Normocytic anemia
- High (>90fl) Macrocytic anemia

Physiological classification(2)

1- Due to decrease Hb or red cells formation
2- Due to increase red cell destruction or loss

CLINICAL PRESETAION(3)

A)**Asymptomatic**: discovered during screening
B) **Symptomatic:**
Stable:

- Pallor of the skin&mucous membranes
- Easy fatigability.
- Poor concentration

Critically ill

• Severe pallor
• Congestive heart failure
• Irritability or drowsiness

common causes of anemia :(4)

1- Inadequate dietary intake of iron especially in:

• Infants in the postnatal period as neither breast milk nor cow's milk contain
adequate amount of iron.
• High carbohydrate diet, excessive milk ingestion > 24 oz /day.
• The onset of IDA usually between 9-24 m of age being earlier in preterm
babies

2- Increased physiological requirement

Infancy due to rapid growth, this can be aggravated by
• Prematurity
• Infection
• Delayed mixed feeding
• Adolescents of both sex due to rapid growth, menstrual loss in females ,intense exercise conditioning as in competitive athletes in high school

3 - Chronic blood loss in older children

• G.I.T. : milk protein inflammatory colitis , hook worm infestation , H. pylori infection , aspirin ingestion ,H.H. ,M. diverticulum ,polyp , hemingeoma ,Ulcerative colitis, chronic diarrhea .
• Urinary tract : Hematuria
• Skin : eczema
• Massive bleeding in hemophilia

4- Malabsorption syndromes

• Cystic fibrosis
• Celiac Disease
• Fever

Congenital heart diseases (CHD):

Classification; (5)

CYANOTIC:

account to 1/3, they are more serious & presented early in life (except TOF presents late).
-they are difficult to diagnose as they are similar to respiratory diseases & chest X–ray is mandatory & we can see one of 2 patterns:

a. plethoric lung =↑ pul-blood flow, e.g TGA (transposition of great arteries), total anomalies of pul–vascular drainage, or truncusarteriosus.

b. oligaemic lung =↓ pul. blood flow, e.g TOF, tricuspid atresia, pul-atresia.

ACYANOTIC:

more common & accounts for 2/3 of CHD, & it is either:
a. Obstructive: PS, AS, COA.
b. Shunt defect: including VSD, ASD, PDA.

Table 2- classification of CHD :

Cyanotic CHD	Acyanotic CHD
Ventricular septal defect Atrioventricular septal defect Patent ductusarteriosus Aortic stenosis Coarctation of aorta Aortic insufficiency	Tetralogy of falot Transposition of great artery Tricuspid atresia Pulmonary atresia

Clinical Picture of CHD :(5)

Usually CHD can present antenatal, neonatal, during infancy or even later in life:

- Common presentation:

1. Heart murmurs
2. Heart failure
3. Cyanosis

- Uncommon or rare presentation:

1. Arrhythmia
2. Hypertension
3. Stroke or embolism
4. SBE (subacute bacterial endocarditis)
5. Recurrent chest infection

Anemia in patients with CHD :

ANEMIA is an important risk factor for morbidity and mortality in patient with cyanotic and acyanotic congenital heart disease (CCHD,ACHD). (6)

ACHD heart failure may occur and worsen by anemia as comorbidity(6)

In CCHD with right to left shunt, arterial oxygen saturation decreases and RBCs count may reach to high level and hyperviscosity develops. in addition , in anemic patients especially those with microcytic iron deficiency anemia , permeability of microcytic erythrocyte decreases in comparision to normocytic cells , therefore thromboembolic and cardiovascular events are encountered more commonly . (7)

In CCHD, normal hemoglobin represents relative anemia and may have disastrous effects.(6,7)and the role of anemia in the management of heart failure and increasing risk of thromboembolic events and hypercyanotic spells in CCHD has been well recognized .(7)

This study is performed to determine the prevalence of anemia in pediatric patients with different congenital heart diseases. (6)

An early detection and an appropriate treatment of anemia in patients with acyanotic heart disease who are presented with heart failure have been strongly recommended. In addition, the prevention of thromboembolic events and cyanotic spells in children with cyanotic CHD have been emphasized (8)

In industrialized countries, cyanotic CHD are currently operated in neonatal or infant period with optimal nutritional support. Whereas, in developing countries , an important number of children with complex CHD are not operated or completely operated. On top of it, the highprevalence of malnutrition is still a real public health concern (9).We would speculate that IDA is of increased rate in this vulnerable group. Anemia in children with CHD, especially in cyanotic children who show high hematocrit value due to chronic hypoxia, is frequently missed or underdiagnosed in daily practice. (10)

Children with cyanotic heart disease have deficient oxygen transport to tissues that might be complicated by polycythemia with the potential risk of brain injury and abnormal haemostatic mechanisms, thrombosis or bleeding diasthesis.(11)

Patients AND METHODs

This was a prospective study conducted from 15th of November 2018 to 7th of January 2019 At Al-Imamain Al-Kadhimain medical city. The study included 60 neonate patients who admitted to the pediatric ward. The neonates were examined at the hospital if they have congenital heart diseases or not . the neonates with suspension of congenital heart diseases were sent for Echocardiography and looking for presence or absence of the disease.

After completing data collection , data (name , gender, the age at delivery , presence and type of C.H.D) were allocated regarding the questionnaire form [see page 21], and packed into groups to simplify their insertion calculation regarding the type of C.H.D.

RESULTS

The study sample included 60 patients presented with congenital heart disease .*(55%) of the patients were males and (45%) were females*.

The Majority of patients (48.33%) were above 1 year age .

Tables 3 and 4 show the age and sex characteristics of the patients.

Table-3 :the sex distribution of patients with CHD.

Sex	*Frequency*	*Percent*
Male	*33*	*55%*
Female	*27*	*45%*
Total	*60*	*100%*

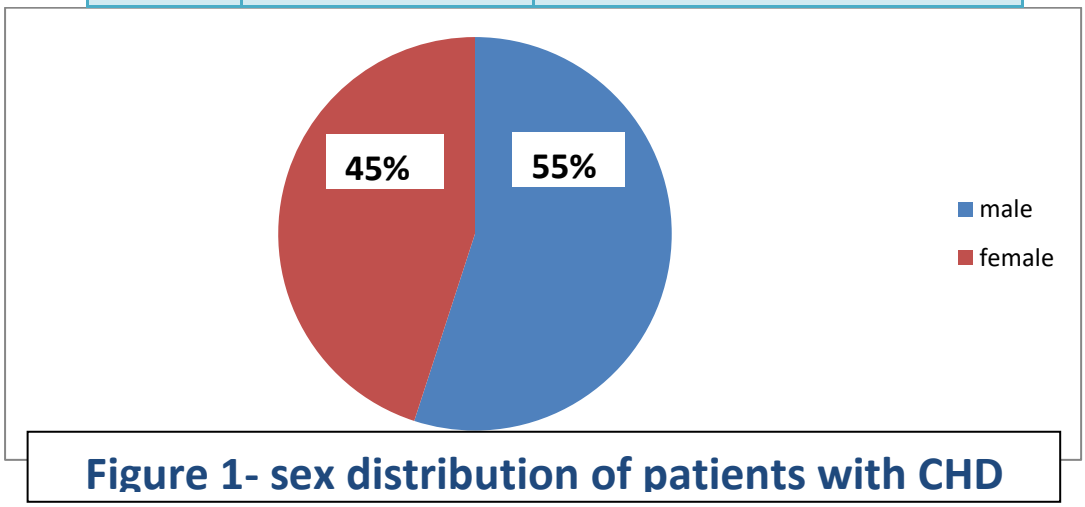

Figure 1- sex distribution of patients with CHD

Table-4 : Age distribution of patients with CHD.

Age	No.of patient	Percent%
Neonate	**9**	**15%**
Infant	**22**	**36.67%**
Above 1 y	**29**	**48.33%**
Total	**60**	**100%**

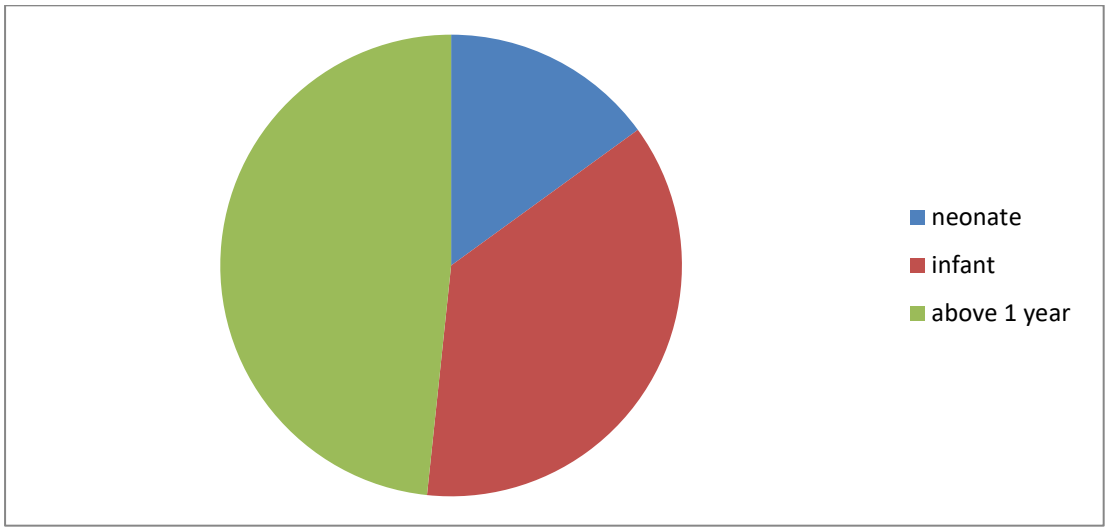

Figure 2- age distribution of patient with CHD.

- Table-5 shows the prevalence of anemia in children with CHD. Depending on Hb concentration 10% of neonate patients with congenital heart disease are anemic with Hb concentration less than 18 mg⁄dL and 5% are not anemic, and 15% of infant patients with congenital heart disease are anemic with Hb less than 9.5mg⁄dL.while 33.3% were anemic with Hb concentration less than 13.5 mg/dl.

Table-5 prevalence of anemia in children with CHD.

Prevalence of anemia	Anemic	Non-anemic	Total
Neonate	6(10%)	3(5%)	9(15%)
Infant	15(25%)	7(11.6%)	22(36.6%)
Above one year	20(33.3%)	9(15%)	29(48.3%)
Total	41(68.3%)	19(31.6%)	*60(100%)*

Regarding the family history of Congenital heart disease(Table -6)

- 60% of patients have positive family history of CHD.
- 40% of patients have negative family history of CHD.

Table 6- family history of patients with CHD.

Family history	*No. of patients*	*Percent (%)*
Positive	36	60%
Negative	24	40%
Total	60	100%

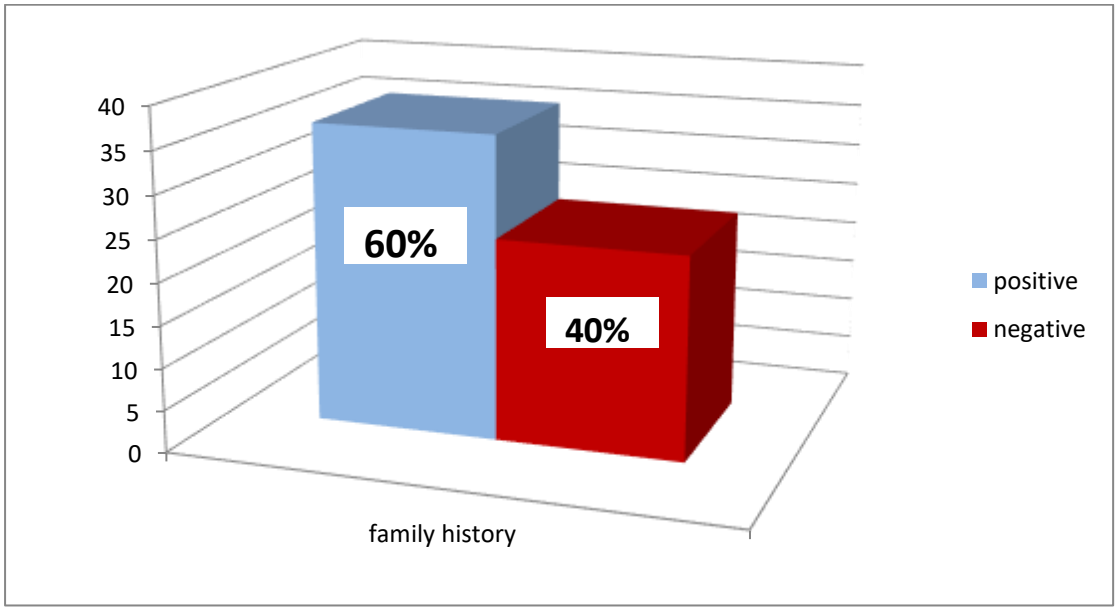

Figure4- family history of patient with CHD.

- Table -7 shows the type of CHD. (cyanotic or Acyanotic). 60% of patient with cyanotic CHD, and 40% of patients with A cyanotic CHD. Cyanotic with anemic and not anemic were 25% and 11%, respectively. Acyanotic with anemic and not anemic were 16% and 8%, respectively. The results were statistically significant since the p-value was 0.03 for cyanotic and 0.04 for acyanotic.

Table-7: Type of CHD whose anemic or not.

Type of CHD	Anemic	Not Anemic	Total	p-value
Cyanotic	25(41.3%)	11(18.7%)	36(60%)	0.03
Acyanotic	16(26.6%)	8(13.4%)	24(40%)	0.04
Total	41(68.3%)	19(31.7%)	60(100%)	

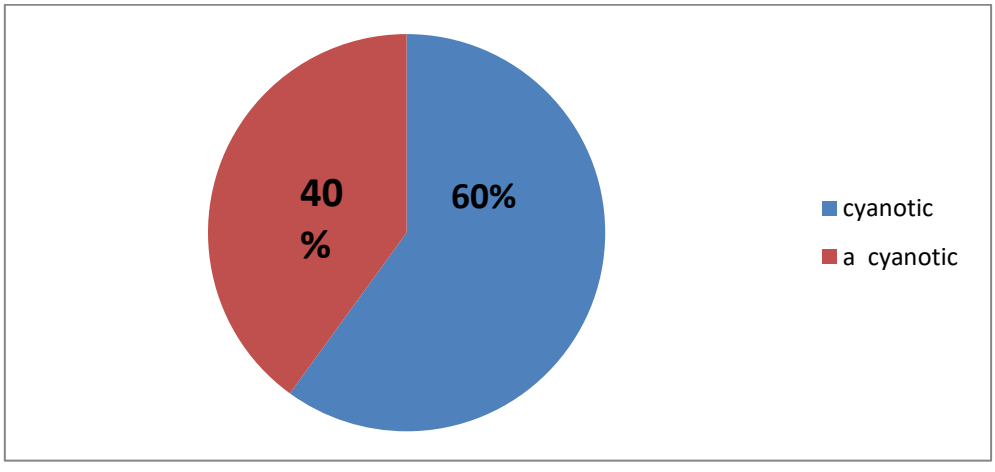

Figure5- type of CHD.

Table-8: percentage of heart failure as complication in CHD patients

Heart failure	*Acyanotic*	*Cyanotic*	*Total*	*p-value*
Positive	12(20%)	7(11.6%)	19(31.6%)	0.02
Negative	12(20%)	29(48.3)	41(68.4%)	0.03
Total	24(40%)	36(60%)	60	

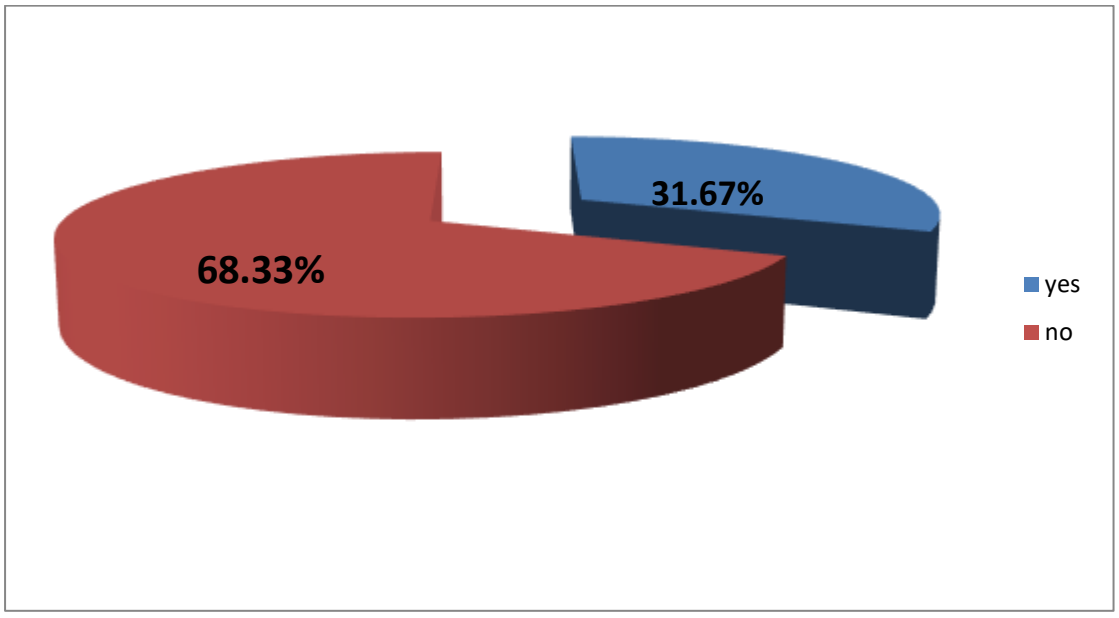

Figure-6: percent of heart failure in CHD patients.

- Table-9 shows the patients who receive treatment and the patients who don't.

Table-9 : percent of patients on treatment.

Receive treatment	*No. of patients*	*Percent (%)*
Yes	38	63.33 %
No	22	36.67%
Total	60	100%

Only 63.3% of patients are on treatment of CHD.

Disscussion

Anemia was relatively common in this population of cyanotic CHD patients. Low MCV and Hb concentration were significant predictors of anemia, suggesting a possible role of iron deficiency and of the heart failure syndrome in its pathogenesis. Anemic CHD patients were at a 3-fold risk of death, even after adjustment for functional class, systemic ventricular function, and other established risk factors.

The prevalence of anemia in CHD. The prevalence of anemia in this CHD children appears to be lower than that reported for acquired heart failure , even though reported estimates of the prevalence of anemia in acquired heart disease vary widely (ranging between 9% and 79%) compared to (J Am Coll Cardiol 2009;54:2093–100) © 2009 by
the American College of Cardiology Foundation

in our study the overall prevalence of anemia was 68.3% anemic, which is almost similar to what was found in London, united kingdom by Gerhard-Paul Diller, et al(12) where they reported a prevalence of 55.9%.

Interestingly, in our study the greatest number of patients were above 1 year age were 20 patient were above 1 year. Similar to Study done in Iran by Amoozgar H, Soltani M ,et al(13) . which include a total of 40 child with CHD were 19 of them were anemic above 1 year age (between 6-12 years old) . and unlike the study done in Italy by Drossos et al.(14) were the bulk of anemic child were neonates.

Regarding gender of the patients, in our study the incidence of CHD was more in male patients 55% male and 45% female similar to what was found in Australia by Christy A N Okoromah, et al(15). were CHD found to be more in male patients also with ratio of male :female of 1.4**:**1 .

Talking about type of CHD, in our study 36 of patient were cyanotic and of those 25 of them were anemic , and 24 are Acyanotic and 16 of them are anemic, which mean the number of cyanotic CHD is more than Acyanotic CHD. This is unlike the study done in Iran by H Amoozgar , et al. (13). Which include 100 patient and the number of Acyanotic were 60 patients more than the cyanotic which was 40 patients.This difference maybe because of the regional variation which make the results differ worldwide between the countries.

Regarding the complications of CHD (table 8) heart failure was found in 31.6% of the patients , 20% of them are with Acyanotic CHD and 11.6% are cyanotic CHD, and the remaining 68.4% of the patients don't have heart failure as complication. And we study this table to know the prognostic power of anemia in the outcomes of CHD patients .
The prognostic power of anemia may derive from its relation to disease severity and exercise capacity (4,6,11).
Anemia results in reduced oxygen-carrying capacity and a premature shift to anaerobic metabolism during exertion. Anemia may also precipitate **heart failure** and cause deterioration in exercise capacity by increasing venous return and reducing oxygen delivery to the myocardium(16).

Regarding treatment**(table 9)** 63.33% of patients are on treatment which mean they are symptomatic and need treatment,
In this population, anemia was a strong and independent prognostic marker. Screening for anemia should become part of the routine assessment of CHD patients as a measure of risk stratification. Correctable causes of anemia, such as bleeding, should always be sought and treated(17–19). Erythropoietin and iron administration have resulted in reduction of symptoms, improvement of exercise tolerance. Whether or not chronic treatment of anemia with iron supplementation and erythropoietin leads to an improvement in outcome in CHD patients needs to be established.
While 36.6% are asymptomatic and not on treatment.

Study limitations. Increased hemoglobin levels in cyanotic patients represent an appropriate physiological adaptation to chronically low oxygen saturations. Iron deficiency “relative anemia” is frequent in cyanotic patients, but occurs at hemoglobin levels much higher than those of noncyanotic individuals, and its diagnosis requires information in addition to mere hemoglobin concentration (e.g., transferring saturation and ferritin levels) (20)Thus, a uniform definition of anemia across the entire CHD spectrum is not feasible.

Although not every single patient seen in our center during the study period underwent blood testing, this was more likely due to patient preference rather than physician choice. Thus, a selection bias cannot be excluded.

Conclusion

Anemia is not uncommon 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.

Recommendations

Future, larger prospective studies with longer follow-up and including patients who are not under tertiary care may provide additional information on anemia mechanisms as well as its prognostic value in CHD patients in general and specific CHD diagnostic subgroups in particular.

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Questionnaire

Patient's age : Neonate (birth to 1 month) ☐

Infant (1month- 1 year ☐

Above 1 year ☐

patient's gender: Male ☐

Female ☐

Mode of delivery: C/S ☐ Vaginally ☐

Mother's age :below 35yr ☐ above 35yr ☐

Father's age : below 35yr ☐ above 35yr ☐

Family history : Yes ☐ No ☐

Admission to the NCU : Yes ☐ No ☐

Type of CHD : Cyanotic ☐ Acyanotic ☐

Hb : below 18 mg/dl ☐ >= 18 mg/dl ☐

PCV : Low ☐ Normal ☐ High ☐

Heart failure : Yes ☐ No ☐

Type of anemia :

Receive Rx : Yes ☐ No ☐