Journal of Cardiovascular Diseases & Diagnosis

Nour et al., J Cardiovasc Dis Diagn 2019, 7:2
DOI: 10.4172/2329-9517.1000358

Research Article Open Access

The Impact of Short Term *Vs.* Extended Venesection in Symptomatic Patients with Congenital Cyanotic Heart Diseases: A Single Center Comparative Study

Nour A*, Kamel H and Roshdy A

Cardiology Department, Ain Shams University Hospital, Cairo, Egypt

Abstract

Background: Secondary polycythemia in patients with Congenital Cyanotic Heart Diseases (CCHD) is associated with many complications starting from iron deficiency anemia up to extensive cerebrovascular stroke. It is noteworthy to say that there is a lot of debate about the agreed protocol for the optimal management of this particular group of patients to obtain the best outcome with less incidence of complications.

Methods: This is a prospective study comparing two different exchange transfusion protocols used for the management of secondary erythrocytosis in CCHD patients. The study included 20 CCHD patients who came to our congenital heart disease unit for elective exchange transfusion over the past 12 months. A custom-made sheet was made including age, diagnoses, number of times for venesection, all hematological parameters before and after the procedure, oxygen saturation and 6-minute walk test.

Results: A total number of 20 patients with CCHD were recruited with mean age of 20.84 years ± 7.4 years with average weight 60 kg. Tetralogy of Fallot was the most common CCHD in the recruited patients (n=5). The average oxygen saturation before the procedure was 75% which improved to 81% after the procedure. Mean hematocrit before the procedure was 70.45% which decreased to a value of 59% after the phlebotomy. A number of 12 out of 20 patients under went venesection of the recommended amount (followed by equivalent isotonic saline replacement) divided equally over an extended period of time of 3 weeks. The remaining 8 patients under went phlebotomy divided over two successive days. There was no significant difference between the 2 groups as regard hemoglobin level and 6-minute walk test, However Among the first arm only one patient developed Iron deficiency anemia versus 7 patients of the second arm.

Conclusion: The extended gradual venesection with adequate volume replacement in patients with CCHD is associated with better outcome as regards iron deficiency anemia.

Keywords: Venesection; Congenital cyanotic heart disease; Iron deficiency anemia

Introduction

The increasing prevalence of Grownups with congenital heart diseases (GUCH) in the last decades could be attributed to the great advances in the field of surgical and medical management of those special population [1]. One of the commonest medical problems that is faced by the pediatric and the adult cardiologist is the secondary polycythemia and hyper viscosity that is a major consequence in patients with congenital cyanotic heart disease (CCHD) [2]. The pathophysiology of this problem is a compensatory mechanism secondary to chronic hypoxia in patients with CCHD due to desaturation. This chronic hypoxemia leads to excess production of erythropoietin and consequently the red cell mass in order to improve tissue oxygenation, however with extreme hypoxia this compensatory mechanism fails as the effect of hyper viscosity overwhelms [3].

The hyper viscosity shifts the oxygen dissociation curve to the left leading to less oxygen delivery to the tissue due to decreased blood flow and tissue perfusion, with the major consequence of increased thrombosis which is associated with increased risk of cerebrovascular stroke [4].

In patients with CCHD increased cell mass is the only underlying mechanism for hyper viscosity, conversely it is associated with thrombocytopenia and iron deficiency anemia [5,6].

Another major problem is that there is no clear guidelines for the optimum management for those patients with CCHD and secondary erythrocytosis [7]. Which is more clinically relevant and associated with better outcome either to depend on hemoglobin level, hematocrit level or the symptoms of the patients as an indicator for the need of venesection, and how to carry on the phlebotomy. Similarly, L swan stated in the European heart journal in 1997 that the practice of venesecting patients with CCHD varies greatly and policies in many hospitals do not reflect, the minimal benefits and considerable risks associated with recurrent venesection [8].

Methods

The current study included 20 patients with CCHD or Eisenmenger syndrome who presented to Cardiology department in Ain shams university hospital, which is a tertiary referral center with a congenital and structural heart disease unit, for clinical and medical follow up over a period of 12 months.

All 20 patients were symptomatic, presented with wide scale of symptoms starting from headache, dizziness, blurring of vision ending up with dyspnea, fatigue and exercise intolerance with hematocrit

***Corresponding author:** Amira Nour, Cardiology Department, Ain Shams University Hospital, Abbassya, 10 Mohamed Helal, Street 5th District, El-Obour city, Cairo, Egypt, Tel: 202-01001486012; E-mail: princess_cardiology@hotmail.com

Received January 23, 2019; **Accepted** February 21, 2019; **Published** February 28, 2019

Citation: Nour A, Kamel H, Roshdy A (2019) The Impact of Short Term *Vs.* Extended Venesection in Symptomatic Patients with Congenital Cyanotic Heart Diseases: A Single Center Comparative Study. J Cardiovasc Dis Diagn 7: 358. doi: 10.4172/2329-9517.1000358

level ≥ 60 mg/dl. patients who were asymptomatic regardless of their hematocrit level, or patients with primary erythrocytosis were excluded.

Exchange transfusion was done according to the following protocol:

- Volume to be exchanged was calculated by the following equation:

Characteristics	Findings
Mean age (range) in yrs.	20.8 (± 7.6)
Mean weight (range) in kgs	61.5 (± 5.1)
Total amount of blood withdrawn (range) in cc	1086 (± 244)
Total amount of plasma replaced (range) in cc	1086 (± 244)
Amount of venesection in each time (range) in cc	501 (± 138)
Referral diagnosis	
Tetralogy of Fallot	(n=5) (25%)
D-TGA	(n=3) (15%)
DILV	(n=6) (30%)
DORV	(n=2) (10%)
Tricuspid atresia	(n=3) (15%)
Eisenmenger	(n=1) (5%)
Symptoms	
Fatigue	(n=9) (45%)
Dyspnea	(n=5)-25%
Headache	(n=4)-20%
Paresthesia	(n=2) (10%)
Previous surgery	
Glenn shunt	(n=3) (15%)
Glenn and Fontain shunt	(n=1) (5%)
Left MBT shunt	(n=1) (5%)
PA banding	(n=2) (10%)
PA banding and Glenn	(n=1) (5%)
None	(n=12) (60%)
D-TGA: D-transposition of Great Vessels, DILV: Double Inlet Left Ventricle, DORV: Double Outlet Right Ventricle, MBT: Modified Blalock Taussing Shunt, PA: Pulmonary Artery.	

Table 1: Showing the demographic and clinical data for the study population.

Demographic and clinical data	N	Mean	SD	Minimum	Maximum
Age	20	20.840	7.6521	0.800	38.000
Weight	20	61.550	5.1654	55.000	75.000
Amount of venesection in each time	20	501.500	138.3845	80.000	750.000
Total amount of blood withdrawn	20	1086.000	244.1397	270.000	1400.000
Total amount of plasma replaced	20	1086.000	244.1397	270.000	1400.000

Table 2: Showing the demographic and clinical data.

Cardiac diagnosis	Number	Diagnosis
Tetralogy of Fallot	5	25.0%
D-TGA	3	15.0%
DILV	6	30.0%
DORV	2	10.0%
Tricuspid atresia	3	15.0%
Eisenmenger	1	5.0%
Total	20	100.0%

Table 3: Showing the different cardiac diagnosis of the study population.

Symptoms	Number	Percentage
Fatigue	9	45.00%
Dyspnea	5	25.00%
Headache	4	20.00%
Paresthesia	2	10.00%

Table 4: Showing the different symptomatology of the study population.

Volume (mL)=Initial Hct – Desired Hct × Weight (kg) × 90 mL/kg/Initial Hct

Desired Hct was calculated as 55%.

- Isotonic saline (0.9% NaCl) was used for partial exchange transfusion.
- Informed consent explaining the potential complications of the procedure for the patients (as thrombosis and infections) from all patients.
- Antibiotic prophylaxsis against infective endocarditis.

Previous surgery	Number	Percentage
Glenn Shunt	3	15.0%
Glenn Shunt and Fontain	1	5.0%
Left MBT Shunt	1	5.0%
PA Banding	2	10.0%
PA Banding, Glenn	1	5.0%
None	12	60.0%
Total	20	100.0%

Table 5: Showing the previous cardiac surgeries for the study population.

Hematological and functional variables	Group Type		Paired T test	p
	Before	After	t	
Hemoglobin	20.800 ± 3.3966	16.1 ± 1.3727	5.737	<0.0001
Hematocrit	70.45 ± 3.2032	58.5 ± 2.0901	-13.973	<0.0001
MCV	89.9 ± 2.5935	82.6 ± 5.1031	-5.703	<0.0001
oxygen saturation	0.746 ± 0.04672	0.81 ± 0.03987	4.66	<0.0001
6 min walk test	224.211 ± 34.2078	292.632 ± 29.2199	-6.629	<0.0001

Table 6: Showing the effect of exchange transfusion in the whole study group before and after venesection.

Venesection Variables	Group Type		Paired T test	
	Group 1 (60%)	Group 2 (40%)	T	p
Amount of venesection in each time	440 ± 123.6564	593.75 ± 108.35	2.856	0.0105
Total amount of blood withdrawn	1118.33 ± 299.6	1037.5 ± 127.47	-0.716	0.4832
Total amount of Saline replaced	1118.33 ± 299.6	1037.5 ± 127.47	-0.716	0.4832

Table 7: Comparing venesection variables in the two groups.

Hematology and Functional Parameters	Group Type		Paired T test	
	Group 1	Group 2	t	p
Baseline Hb	21.5 ± 3.5548	19.75 ± 3.0589	-1.137	0.2702
Hb after	16.417 ± 1.4434	15.625 ± 1.1877	-1.285	0.2151
Oxygen sat before	0.73 ± 0.04786	0.77 ± 0.03505	2.022	0.0583
Oxygen sat after	0.831 ± 0.04274	0.796 ± 0.02416	2.117	0.0484
Hematocrit before	71.417 ± 3.528	69 ± 2.0702	-1.739	0.0992
Hct after	57.375 ± 1.5448	59.286 ± 2.3867	-2.143	0.046
MCV before	89.25 ± 2.5271	90.875 ± 2.5319	1.408	0.1762
MCV after	85.417 ± 3.4234	78.375 ± 4.2741	-4.085	0.0007
6mn walk test before	223.636 ± 38.5416	225 ± 29.761	0.0834	0.9345
6 min walk test after	294.545 ± 33.5749	290 ± 23.9046	-0.326	0.7481
% CH 6MN	33.15 ± 11.2906	30.773 ± 8.9571	-0.492	0.6288
DELTA 6 MN	70.909 ± 17.0027	67.5 ± 14.8805	-0.454	0.6556
Delta hb	-5.083 ± 2.5746	-4.125 ± 2.2321	0.858	0.4022
Delta hct	-12.167 ± 3.2706	-11.625 ± 1.7678	0.426	0.675
Delta MCV	-3.833 ± 3.1286	-12.5 ± 4.6599	-4.999	0.0001
Delta sat	0.0658 ± 0.01676	0.0612 ± 0.01959	-0.56	0.5821

Table 8: Comparing the different hematological variables in the two groups.

- Two peripheral cannulas were inserted, one arterial and one venous.
  - ✓ The arterial cannula is for blood withdrawal.
  - ✓ Venous cannula for saline replacement.
- Start blood withdrawal after simultaneous infusion with saline.
- Blood pressure, PH and oxygen saturation were measured before and after the procedure. CBC was done at base line and 1 week after the procedure.
- Monitor the vital signs thought the procedure and if any problem occurred the procedure was discontinued.

This procedure was done according to the intensive care nursery house staff manual at the UCSF medical center in the university of California [9].

Patients were divided into two subgroups according to the protocol used for exchange transfusion. The first subgroup underwent exchange transfusion over an extended period of time i.e., not more than 500 cc once per week to be repeated every weak until the recommended amount is withdrawn to reach the desired hematocrit (<60%), the second group underwent exchange transfusion over two consecutive days.

Data collected from all the patients after informed written consent for venesection and for inclusion in the study, including:

- Detailed history taking: Personal history, history of present illness, past history including that of cerebrovascular stroke.

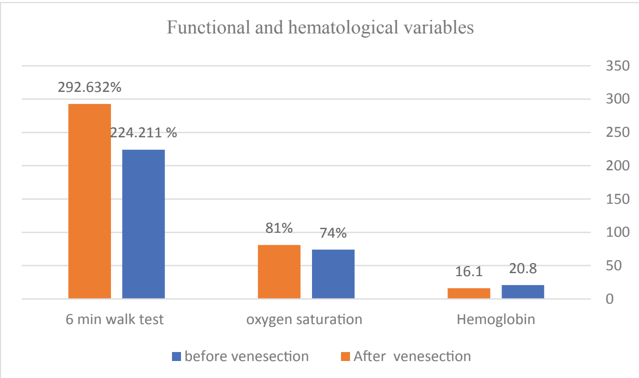

Figure 1: Column graph comparing the effect of exchange transfusion on 6 min walk test, oxygen saturation and Hb level.

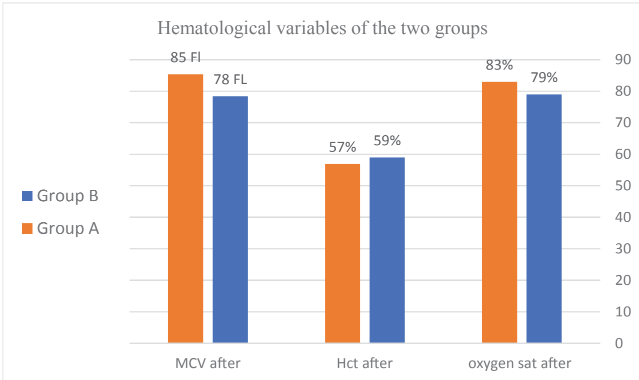

Figure 2: Comparing the different hematological variables in the two groups.

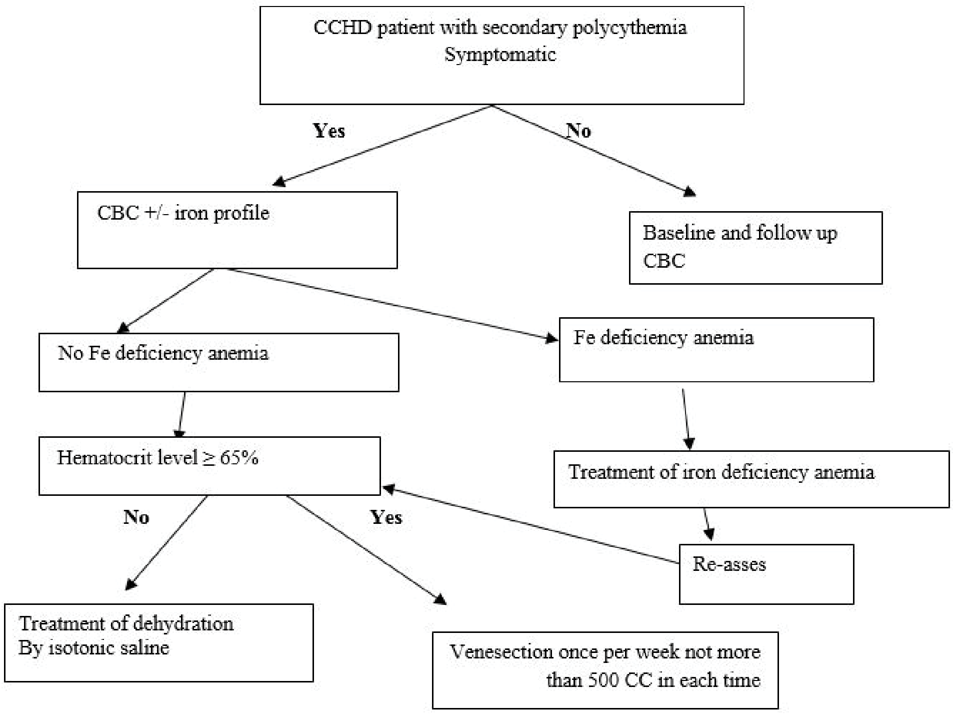

Figure 3: Showing algorithm approach to CCHD with polycythemia.

- Cardiac diagnosis, symptoms at presentation, NYHA class, medications, echocardiographic data, previous cardiac surgeries.

All patients enrolled in the study underwent 6-minute walk test at baseline and one week after completion of the exchange transfusion. Complete blood picture with differential count including MCV, MCG and MCHC was collected at baseline and one week after completion of exchange transfusion. Oxygen saturation by pulse oximetry was also recorded at baseline and at follow up.

Results

The study group included 20 patients with mean age of 20.8 ± 7.6 years, mean weight 61.5 ± 5 kgs, the total amount of blood withdrawn was 1086 ± 244 cc with equal amount of replacement by saline, the mean amount of venesection in each time was 501.5 cc ± 138.

Tetralogy of fallot accounted for the most common cardiac diagnosis (25%) among the study population, fatigue was the most common symptom at the time of presentation, while Glenn shunt was the most cardiac surgery. Patients demographic and clinical data are listed in Tables 1 and 2.

Regarding the effect of exchange transfusion on the study group there was significant improvement of hemoglobin level, hematocrit level, oxygen saturation and 6-minute walk test post exchange transfusion. p value <0.0001) (Table 3 and Figure 1).

We divided the study population into two groups: group (A) included 12 patients who underwent long term extended exchange transfusion (60%) and group (B) included 8 patients who underwent exchange transfusion over two consecutive days (40%). The mean age in group (A) was 19.8 years versus 22 years in group (B), there was no statistical difference between the total amount of blood withdrawn 1118 ± 299 cm^3 in group (A) *vs.* 1037.5 ± 127 cm^3 in group (B),however the amount of venesection in each time was significantly lower in group (A) 440 ± 123 cm^3 *vs.* 593 ± 108 cm^3 in group (B) (p- value=0.01) (Table 4).

Post exchange transfusion oxygen saturation significantly improved in group A with average value of 83% versus 79% in group B (p-value=0.04), similarly the hematocrit level was significantly lowered in group A (57.3 ± 1.5) than group B (59.28 ± 2.3) (p-value 0.04), on the contrary the mean corpuscular volume was significantly reduced in group B (p-value 0.0007), however there was no statistical difference between the two groups as regards hemoglobin level and 6-minute walk test (Table 5 and Figure 2).

Based on data of the current study an algorithm for the management of patients with polycythemia secondary to CCHD was adopted (Tables 6-8 and Figure 3).

Discussion

In our single tertiary Centre study, we tried to set a rational approach and guidelines for the proper management of secondary erythrocytosis in patients with CCHD.

In our study we only managed patients who were symptomatic and with hematocrit level >65%, which was the same recommendations stated by S. Thorne and his co-workers in Grown up Congenital heart disease unit in Royal Brompton hospital in 1998 [2].

An important finding is that fatigue and dyspnea were the most common symptom rather than symptoms of hyper viscosity as headache, dizziness and blurring of vision, this is most probably attributed to that the underlying pathology in CCHD patients with secondary erythrocytosis is tissue hypoxia which lead to increase in the red cell mass only without increase in other blood components such as thrombocytosis, fibrinogen which is the case in primary erythrocytosis (PV) [10].

A unique data in our present work is that we provided the underlying diagnosis for the patients undergoing venesection, where the tetralogy of Fallot (unrepaired) was the most common diagnosis, followed by D-TGA, DILV, DORV then only one Eisenmenger patients, this can be explained by that the Fallot patients who reach adulthood without any previous cardiac surgeries has more severe RVOT obstruction which lead further hypoxemia, increase right to left shunt with shift of the oxygen dissociation curve to the left leading to a vicious cycle of decompensated erythrocytosis [11].

It is to be noted that two third of the patients in our study has no pervious cardiac surgeries, while the remaining one third who has previous cardiac surgeries had pulmonary hypertension which also increase the risk of erythrocytosis due to chronic hypoxemia [12].

In our study we compared the two applied protocols as regards hematological and functional variables we found that both protocols were equivalent as regards improvement in functional capacity (assessed by 6 min walk test), hemoglobin, hematocrit. Consequently in 2008 the American college of cardiology/American heart association published guidelines and recommended performing therapeutic phlebotomy for symptomatic patients with hematocrit level more than 65% and hemoglobin more than 20 g/dl [7].

The clinical parameters used for evaluation of patients post venesection showed improvement in symptoms of patients 1 week later, increase in oxygen saturation and improvement in six-minute walk test 1-2 weeks after the procedure. This is supported in literature by the fact that venesection also results in reduced peripheral vascular resistance, increased stroke volume, cardiac output and systemic blood flow [13,14]. Similar to our study Oldershaw & Sutton stated that repeated exercise test 2 weeks after venesection showed increased oxygen uptake and reduce oxygen debt [14]. The controversy here arises as excessive and frequent venesection to improve symptoms may render those patient hypoxic and anemic, reducing tissue oxygenation and exercise tolerance [15].

It was thought previously that secondary erythrocytosis is associated with increased risk of cerebrovascular stroke, as the neurological symptoms of hyper viscosity can be misinterpreted as cerebrovascular stroke [16]. In our study there was no increase in the incidence of cerebrovascular stroke in both groups similar to Perloff et al., who didn't observe any increase in the incidence of stroke in adult patients with CCHD who were followed up for 12 years [16], in addition to Ammash and his coworkers who proved that incidence of CVS is not related to the hemoglobin or hematocrit level but rather to repeated phlebotomies, hypertension and atrial fibrillation [9].

In our study it was clear that Group B (who underwent venesection of the recommended amount over two successive days develops iron deficiency anemia compared to group A (who underwent venesection of the recommended amount over long term period once every week), it is known that patients with CCHD who underwent repeated phlebotomies are at risk of developing iron deficiency anemia which increase the risk of hyper viscosity and CVS as the iron deficient RBCs are more rigid and less deformable so increase the hyper viscosity [17].

Study limitation and recommendations

Venesection is not a benign procedure as it may lead to hemodynamic upset and iron deficiency anemia. The lack of other therapeutic options makes it the only solution provided that a well-designed protocol makes the benefits outweighs the risks.

Further studies with longer follow up of the patients to reveal the clinical predictors for the frequency of venesection and relapse post venesection is needed.

Conclusion

The extended gradual venesection with adequate volume replacement in patients with CCHD is associated with better outcome as regards iron deficiency anemia and equally effective in improving functional capacity compared to a rapid exchange transfusion protocol.

References

1. Bhatt AB, Elyse F, Karen K (2015) Congenital heart disease in the older adult. Circulation 131: 1884-1931.
2. Thorne SA (1998) Management of polycythemia in adults with congenital cyanotic heart disease. Heart BMJ 79: 315-316.
3. Rose SS, Shah AA, Hoover DR (2007) Cyanotic congenital heart disease with symptomatic erythrocytosis. J Gen Intern Med 22: 1775-1777.
4. Swan L, Birnie DH, Hillis WS (1997) The hematological management of patients with cyanotic congenital heart disease: A time for consensus. European Heart Journal 18: 1973-1976.
5. Mossuz P, Girodon F, Donnard MM (2004) Diagnostic value of serum erythropoietin level in patients with absolute erythrocytosis. Haematologica 89: 1194-1198.
6. Warrell DA, Cox TM, Firth JD (2003) Cyanotic heart disease: A multisystem disorder. Oxford Textbook of Medicine, 4th edition. London: Oxford University Press.
7. Territo MC, Rosove MH (1991) Cyanotic congenital heart disease: Hematologic management. J Am Coll Cardiol 18: 320-322.
8. Ammash N, Warnes CA (1996) Cerbrovascular events in adult patients with cyanotic congenital heart disease. J Am Coll Cardiol 28: 768-772.
9. UCSF (2004) Children's hospital at USCF medical center. Polycythemia / Hyperviscosity. The Regents of the University of California 2: 1.
10. Kwaan HC, Wang J (2003) Hyperviscosity in polycythemia vera and other red cell abnormalities. Semin Thromb Hemost 29: 451-458.
11. DeFilippis AP, Law K, Curtin S (2007) Blood thicker than water, the management of adults with cyanotic heart disease. Cardiol Rev 15: 31-34.
12. Warnes CA, Williams RG, Bashore TM (2008) ACC/AHH 2008 guidelines for management of adults with congenital heart disease. J Am Coll Cardiol 52: e143-e263.
13. Rosenthal A, Nathan DG, Marty AT (1970) Acute hemodynamic effects of red cell volume reduction in polycythemia of cyanotic congenital heart disease. Circulation 42: 297-308.
14. Oldershaw PJ, Sutton MG (1980) Haemodynamic effects of haematocrit reduction in patients with polycythaemia secondary to cyanotic congenital heart disease. Br Heart J 44: 584-588.
15. Somerville J (1997) Management of adults with congenital heart disease: An increasing problem. Annual Review of Medicine 48: 283-293.
16. Perloff JK, Marelli AJ, Miner PD (1993) Risk of stroke in adults with cyanotic congenital heart disease. Circulation 87: 1954–1959.
17. Chamanian S, Malek M, Rohani A (2015) Hematologic abnormalties in cynaotic congenital heart disease patients. Journal of Cardio-thoracic Medicine 3: 270-272.