

## HAEMATOLOGICAL CHANGES FOLLOWING OPEN HEART SURGERY

Mahfuz H<sup>1</sup>, Rahman MM<sup>2</sup>, Mahmud Z<sup>3</sup>, Khan MM<sup>4</sup>**Abstract**

**Introduction:** Cardiopulmonary bypass surgery is a well known technique in open heart operation. Out of all open heart surgery cases CABG (coronary artery bypass graft) comprises the maximum number. In the United States, surgeons perform approximately 250,000 CABG procedures each year. In Bangladesh though definite data is not available, approximately 3500 patients undergo open heart surgery each year.

**Objective:** The aim of the study was to find out the hematological changes that may occur during and immediately after open heart surgery and to find out the necessary remedial measures so as to reduce the morbidity and mortality.

**Methods:** This prospective study was carried out at Armed Forces Institute of Pathology (AFIP), Cardiac Centre, Combined Military Hospital (CMH), Dhaka Cantonment and Heart Foundation Hospital and research Institute, Mirpur, Dhaka over a period of 02 months. Randomly selected 30 patients of all age and sex, who were undergoing CABG, repair of heart vales, Atrial Septal Defect (ASD) and Ventricular Septal defect (VSD) were included in this study. Seven hematological parameters of these patients were done before, during and after operation by automated hematology analyzer "Cell Dyn 3700 Abott USA" and automated coagulometer "ST-4". The results of these parameters were compiled and analyzed using Microsoft excel and SPSS.

**Results:** The mean hemoglobin level 01 hr before operation was 13.8 g/dl and 04 hr after operation was 13.0 g/dl respectively. Mean±SD change in hemoglobin level between 01 hour before operation and 04 hours after operation was 0.84±1.24 gm/dl, which was 6.1% lower than the initial value. Mean±SD TLC rise between before and after operation was 7.7±2.4 x10<sup>9</sup>/L which was 90.8% increase from the initial value (P value<0.001). Mean±SD neutrophils increase was 33±5 which was 60% more from initial value (P value<0.001). Mean±SD platelet count decrease was 122±24 x 10<sup>9</sup>/L which was 40% decrease from the initial value (P value<0.001). Mean free plasma hemoglobin (mg/dl) one hour before open heart operation was 9.2 mg/dl and 77 mg/dl four hours after operation. Out of 30 cases only 04 (13%) cases developed prolonged APTT. D-dimer level was within normal limits in all cases before operation and was increased only in 09 (30%) cases.

**Conclusion:** To reduce the cost and hospital stay of the patients undergoing open heart surgery, rapid recovery should be ensured. This can only be accomplished by taking and rapidly implementing multidisciplinary opinions of cardiac surgeon, cardiologist, cardiac anesthesiologist, transfusion medicine specialist and hematologist.

**Key-words:** Coronary artery bypass graft (CABG), Atrial Septal Defect (ASD), Ventricular Septal Defect (VSD), Total Leucocyte Count (TLC), Activated Partial Thromboplastin time (APTT).

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## Introduction

In open heart surgery, cardiopulmonary bypass (CPB) technique is applied. Cardiopulmonary bypass (CPB) is a technique by which the pumping action of the heart and the gas exchange function of the lung is replaced temporarily by a mechanical device - the pump oxygenator-attached to a patient's vascular system.<sup>1</sup> Although some temporary dysfunction of organs and systems is occasionally the sequelae of present technique, CPB has become an indispensable technique for most cardiac surgical procedure<sup>2</sup>.

The temporary provision of arterial blood flow using a pump oxygenator is an abnormal situation in which most, if not all, of the body's physiologic processes are affected<sup>3</sup>. In total CPB, essentially all systemic venous blood returns to the pump oxygenator instead of heart.

Cardiopulmonary bypass is not physiologic. It is a stress on the body similar to the stress of trauma or surgery itself<sup>4</sup>. It causes several metabolic and hormonal derangements but from hematological point of view, it causes bleeding tendency, hemolysis secondarily to red cell trauma and shear stress, diffuse systemic inflammatory reaction due to activation of Hageman factor<sup>5</sup>. Bleeding is common because of sequestration of platelets, inactivation of coagulation factors from enzymatic injury, as well as fibrinolysis<sup>6,7</sup>.

Other than CPB a number of factors affect hematological values in patient with cardiac surgery. These are drugs like heparin, warfarin, aspirin, diuretics and anti-hypertensive and also abnormal hepatic function, infections and other co-morbid clinical conditions<sup>8</sup>.

In this study, hematological parameters such as Hemoglobin concentration (Hb), Total Leucocyte count (TLC), Differential Leucocyte Count (DLC), Platelet Count (PLT), plasma free haemoglobin, Activated Partial Thromboplastin Time (APTT) and D-dimer were analyzed. The aim of the study is to evaluate the hematological changes following open heart surgery and their remedial measures.

## Materials and methods

The study was conducted at National Heart Foundation, Mirpur, Dhaka, Armed Forces Institute of Pathology (AFIP) and Combined Military Hospital (CMH), Dhaka Cantonment from April, 2003 to May 2003. Randomly selected 30 patients of all age and sex were selected for this study. Twenty five patients from National Heart Foundation, Dhaka, Mirpur and 05 patients from CMH, Dhaka Cantonment who were undergoing operation for open heart surgery, Coronary Artery Bypass Grafting (CABG), repair of heart valves, Atrial Septal Defect (ASD) and Ventricular Septal defect (VSD) were included in this study. Patients suffering from severe co-morbid medical conditions, having ejection fraction less than 35% or undergoing emergency interventions or re-operation were excluded from the study. Out of 30 cases, 21 cases have undergone aortocoronary bypass grafting (CABG) and 09 cases have undergone valve repair/ASD, VSD repair.

All patients were maintained on their current drug therapy up to the time of the operation except for aspirin which was withdrawn 7-10 days before operative procedures. Anesthetic and surgical procedures were performed in the standard manner. Before connecting to CPB each patient received 300 U/kg Injection heparin into the central vein to achieve an activated coagulation time (ACT) longer than 400 s. Different bypass devices were used to maintain mild hypothermia (33°C) for CABG and moderate hypothermia (26°C-28°C) for valve surgery. After successful weaning from CPB, Injection protamine (1 %) was administered into a peripheral vein to achieve neutralization of the effects of heparin. Aprotinin or antifibrinolytics were not used during our study. Four milliliters blood samples were collected aseptically from antecubital vein two times, 01 hour before surgery and 04 hours after surgery from every patient included in this study. From each blood sample, 02 ml was delivered into a bottle containing 3.0 mg dried EDTA for analysis of haematological profile (Hb level, plasma free Hb, TLC, DLC and PLT count) and 1.8 ml was added to test tube containing 0.2ml of 3.2% trisodium citrate solution for analysis of coagulogram (APTT and D-dimer).

Immediately after collection all blood samples were sent to AFIP for analysis. Hematological profiles were analyzed in automated cell counter "Cell Dyn 3700" Abott, USA. Coagulogram were analyzed in automated coagulometer "ST- 4". D-dimer was measured by agglutination method. Free plasma haemoglobin was measured by Spectrophotometric method. Before running the samples, these instruments were calibrated by normal, high and low controls provided by the manufacturer.

## Results

Demographic data such as age, sex, smoking, associated disease are shown in Table-I.

**Table-I:** Demographic data of the patients (n=30)

Age group (in years)	Sex		Smoking	Obesity	Associated disease	
	Male	Female			HTN	DM
11 - 62	27	03	16	05	13	12

Parameters which were taken in this study are shown in Table II.

**Table-II:** Hematological parameters taken in this study

Hematological parameters	Unit
Hemoglobin (Hb)	g/dl
Total Leucocyte Count (TLC)	$\times 10^9/l$
Percentage of Neutrophils	%
Total Platelet Count (PLT)	$\times 10^9/l$
Plasma free haemoglobin	mg/dl
Activated Partial Thromboplastin Time (APTT)	Second
D-dimer	ng/dl

Table-III shows the changes in hemoglobin concentration one hour before and four hours after open heart surgery. Mean Hb level one hour before operation was 13.8 g/dl and four hours after operation was 13.0 g/dl.

**Table-III:** Hemoglobin (g/dl) changes 01hour before and 04 hour after operation (n=30)

One hour before operation			Four hour after operation		
Range	Mean	Mean±SD	Range	Mean	Mean±SD
18 - 12.5	13.8	13.8±1.3	15 - 10.5	13.0	13.0±1.4

Mean±SD change in hemoglobin level between 01 hour before operation and 04 hours after operation was  $0.84 \pm 1.24$  gm/dl, which was 6.1% lower than

the initial value. On an average each patient received 3 to 6 units of blood transfusion which increased the hemoglobin level at least 3gm/dl and as such hemoglobin decrease comes to approx 3.8gm/dl which should be 27.8% lower than the initial value (P value<0.001).

**Table-IV:** Differences in hemoglobin (g/dl) changes 01hr before and 04 hr after operation (n=30)

Difference before and after operation		Expected Difference	Expected Decrease (%)	Percentage of Decrease	P-value
Range	Mean	Mean±SD			
3.0 to -1.2	0.84	$0.84 \pm 1.24$ $3.84 (3.0+0.84)$	27.8	6.1	<0.001

The mean TLC one hour before and four hours after open heart surgery was  $8.4 \times 10^9/l$  and  $16.1 \times 10^9/l$  respectively.

**Table-V:** Changes in Total Leucocyte count ( $\times 10^9/l$ ) 01 hr before and 04 hr after operation (n=30)

One hour before operation			Four hour after operation	
Range	Mean	Mean±SD	Range	Mean
12.2 - 5.5	8.4	$8.4 \pm 1.9$	24.5 - 12.6	16.1
				$16.1 \pm 3.2$

Mean±SD TLC rise between before and after operation was  $7.7 \pm 2.4 \times 10^9/L$  which was 90.8% increase from the initial value (P value<0.001) (Table-VI).

**Table-VI:** Differences in Total Leucocyte Count ( $\times 10^9/l$ ) changes 01hr before and 04 hr after operation (n=30)

Difference before and after operation			Percentage of increase after operation	P-value
Range	Mean	Mean±SD		
14.0 - 4.0	7.7	$7.7 \pm 2.4$	90.8	<0.001

The mean neutrophil percentage 01 hour before and 04 hours after open heart surgery were 56% and 90% respectively.

**Table-VII:** Changes in the percentage of neutrophils (%) 01 hr before and 04 hr after operation (n=30)

One hour before operation			Four hour after operation		
Range	Mean	Mean±SD	Range	Mean	Mean±SD
70 - 46	56	$56 \pm 6$	95 - 85	90	$90 \pm 3$

Mean±SD neutrophils increase was  $33 \pm 5$  which was 60% more from initial value (P value<0.001).

**Table-VIII:** Differences in the percentage of neutrophils (%) changes 01hr before and 04 hr after operation (n=30)

Difference before and after operation			Percentage of increase after operation	P-value
Range	Mean	Mean±SD		
41 - 22	33	33±5	60	<0.001

The mean platelet count ( $\times 10^9/L$ ) one hour before open heart operation was  $297 \times 10^9/L$  and four hour after operation was  $178 \times 10^9/l$ .

**Table-IX:** Changes in platelet count ( $\times 10^9/l$ ) 01 hr before and 04 hr after operation (n=30)

One hour before operation			Four hour after operation		
Range	Mean	Mean±SD	Range	Mean	Mean±SD
410- 220	297	297±72	300 - 100	178	178±57

Mean±SD platelet count decrease was  $122 \pm 24 \times 10^9/l$  which was 40% decrease from the initial value (P value<0.001).

**Table-X:** Differences in platelet count ( $\times 10^9/l$ ) 01hr before and 04 hr after operation (n=30)

Difference before and after operation			Percentage of decrease after operation	P-value
Range	Mean	Mean±SD		
170 - 100	122	122±24	40	<0.001

Mean free plasma haemoglobin (mg/dl) one hour before open heart operation was 9.2 mg/dl and 77 mg/dl four hours after operation.

**Table-XI:** Changes in free plasma hemoglobin (mg/dl) 01 hr before and 04 hr after operation (n=30)

One hour before operation			Four hour after operation		
Range	Mean	Mean±SD	Range	Mean	Mean±SD
12- 07	9.2	9.2±1.4	91 - 70	77	77±12

Mean±SD free plasma hemoglobin between 01 hour before and 04 hours after operation increased to  $68 \pm 12$  mg/dl, which was 740% increase from initial value (P value<0.001).

**Table-XII:** Differences in free plasma hemoglobin (mg/dl) 01hr before and 04 hr after operation (n=30)

Difference before and after operation			Percentage of increase after operation	P-value
Range	Mean	Mean±SD		
82 - 43	68	68±12	740	<0.001

Mean activated partial Thromboplastin time (APTT) one hour before open heart operation was 35 seconds and 40 seconds four hour after operation. Out of 30 cases only 04 cases developed prolonged APTT which was only 13% of the total cases.

**Table-XIII:** Activated Partial Thromboplastin Time (seconds) 01 hr before and 04 hr after operation (n=30)

One hour before operation			Four hour after operation		
Range	Mean	Mean±SD	Range	Mean	Mean±SD
38 - 30	35	35±2	82 - 30	40	40±13

D-dimer level was measured 01 hour before operation and all the levels were within normal limits. Four hours after operation D-dimer level was increased in 09 cases out of 30 cases.

**Table-XIV:** D-dimer level (ng/ml) 01 hr before and 04 hr after operation (n=30)

One hour before operation	Four hour after operation		Percentage (%) of raised cases
	Normal	Raised	
< 500 ng/ml	21	09 (>500 ng/ml)	30

## Discussion

In open heart surgery, cardiopulmonary bypass (CPB) technique is applied which is a pre-requisite for this procedure. Cardiopulmonary bypass (CPB) is a technique by which the pumping action of the heart and the gas exchange function of the lungs are replaced temporarily by a mechanical device-the pump oxygenator-attached to a patient's vascular system.

Out of all open heart surgery cases CABG comprises the maximum number. In the United States, surgeons perform approximately 250,000 CABG procedures each year<sup>9</sup>. In Bangladesh though definite data is not available, approximately 3500 patients undergo open heart surgery each year.

On an average, CABG takes five to six hour's time to perform. In this procedure, a portion of a vein, usually the saphenous, is used to connect the aorta and the coronary artery distal to the obstruction. The internal mammary artery is commonly used to bypass the most significant lesion involving the left anterior descending artery.

At the initial stage of the operation, the surgeon performs a cardiopulmonary bypass to collapse the lungs and create a bloodless surgical field. This procedure also provides the patient with respiratory support during the operation and maintains circulation. Other important components of CABG procedure include the use of cardioplegia solution to temporarily arrest the heart beat, anticoagulation with heparin and induction of hypothermia by lowering the body temperature to 28°C to decrease the patient's metabolic demand<sup>10</sup>. During the CABG procedure, heparin is administered to achieve an ACT four times normal and the effects of heparin are reversed with protamine sulfate following the procedure. Therefore, eight or nine ACT measurements are typically required before the beginning to the completion of the procedure to monitor coagulation status of the patient<sup>11</sup>.

CPB exposes blood to artificial surfaces causing mechanical trauma from the pump, alterations in temperature and dilution with fluid, transfused whole blood, plasma product and drugs and leads to hemolysis, activation of platelets, coagulation cascade and fibrinolytic system. In addition activation of complement system and increased level of granulocyte components, particularly neutrophils occur<sup>12</sup>. In this study a mean change of hemoglobin level 01 hour before operation and 04 hours after operation is a decrease in Hb concentration by 3.84±1.24 gm/dl which is 27.8% lower than the initial value (P value <0.001). Mean free plasma hemoglobin increased after operation by 68±12 mg/dl which is 740% increase from initial value (P value <0.001).

Before operation mean±SD free plasma Hb level was 9.2±1.4 mg/dl and 04 hours after operation it was raised to 77±12 mg/dl. Han and colleagues found free plasma hemoglobin to be 8.3±1.3 mg/dl before CPB and 90.7±8.4 mg/dl after completion of CPB. The result in this study is almost similar to the study of Han and his colleagues<sup>13</sup>.

A significant change in the TLC mostly due to an increase in neutrophils was observed. Mean±SD TLC was increased after operation by 7.7±2.4X10<sup>9</sup>/L which was 90% more from the initial value (P value <0.001).

Mean±SD neutrophils increased after operation to 33±5%, which was 60% more from initial value (P value <0.001). Riegel and colleagues also found a rise in WBC count to a peak of 12–24x10<sup>9</sup>/L at 24 hours post operatively.

The mean platelet count decreased from 297x10<sup>9</sup>/L before operation to 178X10<sup>9</sup>/L after operation. The mean±SD platelet count decreased by 122±24X10<sup>9</sup>/L which was 40% decrease from the initial value (P value <0.001). Kalter RD and colleagues observed that CPB decreases platelet count about 60% of pre bypass value which is almost similar to the findings in this study<sup>14</sup>.

In the present study only 4 patients out of 30 (13%) developed prolonged APTT after operation. But significant number of patient developed (9 out of 30) fibrinolysis as evidenced by a rise of D-dimer (ng/ml). Percentage of patients who developed fibrinolysis is 30%. Brandtert JT and colleagues showed hyper fibrinolysis in 159 (20%) of 774 patients undergoing bypass grafting which is close to the findings in this study<sup>15</sup>.

### Conclusion

Now-a-days open heart surgery is randomly performed worldwide by the cardiac surgeons. In the United States, surgeons are performing approximately 250,000 CABG procedures each year. We are delighted to mention that Bangladesh is not lagging behind. Successful cardiac surgeries are being done by many centers in this country. We found significant changes in hemoglobin, RBC, TLC, platelets and coagulation profiles due to open heart surgery.

Knowledge of these hematological changes will allow the cardiac surgeons to remain in consultation with a hematologist to take appropriate timely measures to correct these for a successful outcome of open heart surgery.

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