

## PREOPERATIVE ANEMIA INCREASES RISK OF RENAL DYSFUNCTION AFTER CORONARY ARTERY BYPASS SURGERY

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### ABSTRACT:

#### INTRODUCTION:

*Preoperative anemia is commonly encountered in patients undergoing coronary artery bypass surgery. It is now an established fact that anemia at the time of surgery affects the outcome. However, this fact has not been taken into account in the major cardiac surgery risk stratification systems. The impact of preoperative anemia on development of postoperative renal failure is not very well established. This study is planned to evaluate this effect.*

#### AIMS & OBJECTIVE:

*To assess the increases risk of renal dysfunction after Coronary Artery Bypass Surgery in patients having preoperative anemia.*

#### MATERIAL & METHODS:

*This is a retrospective study, data extracted from the patient record operated at our institution between Jan 2019 to Feb 2021 for isolated stable coronary artery bypass surgery. A total of 819 patients were operated, final sample size of 773 patients was selected, 185 (24%) were anemic by world health organization definition of anemia. These patients and various parameters were then compared with non-anemic patients.*

#### RESULTS:

*Preoperative anemia was linked with three times increased risk of developing acute kidney injury or worsening of pre-existing renal dysfunction (18.3% vs 6.4%  $p < 0.0001$ ). A significant difference observed in the anemic and non-anemic groups in developing post-operative stroke (2% vs 1%  $p = 0.008$ ), development of new onset atrial fibrillation (36.2% vs 32.9%  $p = 0.003$ ) and prolonged hospitalization (53.5% vs 35.8%  $p < 0.0001$ ). There was however no effect on post-operative myocardial infarction (2% in each group  $p = 0.09$ ).*

#### CONCLUSION:

*Preoperative anemia is a major contributor in developing renal dysfunction, stroke and atrial fibrillation after coronary artery bypass surgery.*

#### KEY WORDS:

*Anemia, cardiac surgery, CABG, renal dysfunction, stroke.*

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**Author's Contribution:** AI: Concept, design of study, annalysis and interpretation, review of literature. AA: Collection of data tabulation, recording of cases on proforma, review of liturature. TK: Pre operative recording of patient data, study design, interpretation of data and critical review.

## INTRODUCTION:

Anemia has a complex etiology, and is the result of interplay of many diverse factors. Some factors are disease related while others are environmental and related to social and economic development. Anemia itself is not a disease, however the underlying mechanisms contributing to it have complex interplay with many other physiological processes of the body. Preoperative Anemia is a significant contributing factor to the cardiovascular diseases.<sup>1</sup> A number of studies have shown its impact on elderly, in patients with heart failure and patients having coronary heart disease.<sup>1</sup> Almost 1/3rd of the world population is anemic.<sup>2</sup> According to the WHO standards, a large number of anemic patients undergo CABG. The effects of preoperative anemia on mortality and renal dysfunction after cardiac surgery have not been well defined. There are studies that have shown significant impact on in-hospital morbidity and mortality after CABG and valve surgeries.<sup>3-7</sup> However other studies have not shown any effect on adverse cardiac surgery outcomes.<sup>8,9</sup> Kulier et al in a landmark paper have a view that anemia in patients undergoing CABG is an independent predictor of non-cardiac events only, and the cardiac related events are more so influenced by the cardiac related pathologies like myocardial infarction and heart failure etc.<sup>10</sup> EuroScore and STS risk stratification models are the two widely used risk stratification systems in cardiac surgery, both of these models do not consider the preoperative anemia as a factor influencing cardiac surgery risk.<sup>6,11,12</sup> The aim of this research was to assess if the pre-operative anemia affects in any way the clinical outcomes in terms of renal dysfunction in patients undergoing CABG surgery.

## MATERIAL AND METHODS:

This was a retrospective observational study of adult cardiac surgery patients. All consecutive patients undergoing elective CABG from Jan 2019 to Feb 2021 operated at Wazirabad Institute of Cardiology were included in the study. The final sample size was 773, of which of which 185 (24%) had preoperative anemia (Fig. 1). Data was obtained from patient charts, and entered into a purpose designed proforma. Patients whose preoperative hemoglobin level was not known, emergency surgery or patients with preoperative intra-aortic balloon pump, CABG with valve surgery and Redo CABG or preoperative acute renal failure (anuria or output less than 10ml/Hr) were excluded. Data analysis was done by using

SPSS 23.

The primary end point was development of acute kidney injury (AKI), secondary end points were development of new onset atrial fibrillation (AF), post CABG acute myocardial infarction (MI), stroke and duration of hospitalization.

World Health Organization (WHO) defines anemia as hemoglobin level of < 13 g/dl in men and < 12 g/dl in women. Urgent surgical priority was defined as when patient factors require the patient to be operated in the same index hospitalization, while elective surgery was defined when patient factors allowed the patient to be discharged home, and readmitted on a later date for surgery. Acute kidney injury (AKI) was defined as serum creatinine >2 mg/dl or a creatinine level double the preoperative level. Highest creatinine was taken from the patient record after CABG. A diagnosis of postoperative MI was made on appearance of new Q waves, or a 25% reduction in R waves in two contiguous leads on a 12 lead ECG. New onset atrial fibrillation was defined as AF of any duration on the basis of 12 lead ECG and rhythm strip. Stroke was defined as new neurological deficit diagnosed clinically.

The anesthesia and surgical procedure were standard in all cases. All patients continued their medication up to the day of surgery. Hemodynamic monitoring consisted of standard ECG, saturation on pulse oximeter, radial and central venous cannulation. Induction of anesthesia was with 2mg midazolam followed by 0.5mg/kg ketamine and 0.5-1 mg/kg propofol. Atracurium 0.3mg/kg is given before intubation. Anesthesia was maintained by propofol along with nalbuphine, atracurium and isoflurane. The cardiopulmonary bypass was conducted using membrane oxygenator. Priming fluids were 1000ml of Hartman's solution, 500 ml of Gelafundin, 0.5g/Kg mannitol, 7ml of 10% calcium gluconate and 6000 IU of unfractionated heparin. Systemic temperature was kept between 34 and 32 degrees centigrade. Myocardial protection was achieved by intermittent cold 1:4 crystalloid to blood St. Thomas cardioplegia. Cardioplegia was repeated every 15 to 20 minutes along with topical cooling with iced slush. At the end of procedure patients were shifted to intensive care unit.

## STATISTICAL ANALYSIS:

Data analysis was done by using SPSS 23. Continuous variables were expressed as mean +/- standard deviation. Categorical variables were expressed as percentages. Skewness of data was checked before further analysis to ensure

Normal distribution. T2 test was used to determine the significance when comparing anemic vs non anemic groups for categorical variables. Student's t test was used to test for the significance of difference for continuous variables. A CI of 95% was chosen and a p value of < 0.05 was considered significant. Other patient characteristics and confounding parameters were assessed between two groups to reduce the study bias (Table 1).

**RESULTS:**

We studied a sample of 773 patients, among these 185 (24%) were anemic (p<0.001). Female patients were 51(27.7%) in the anemic group compared to 141(23.9%) in the non-anemic group (p<0.001).The mean hemoglobin in anemic group was 11.5 g/dl ± 1.1 compared to 14.3 g/

dl ± 1.1 in the control group. Patients in anemic group were generally older, mean age 69 ± 10.6 years than control group 64.5 ± 11.6 years (p< 0.0001). Hypertension was also common in the anemic group 129 (69.7%) compared to 391 (66.4%) in the control group (p=0.002). Chronic kidney disease and chronic obstructive pulmonary disease were also present in some cases preoperatively. Anemic patients were also more likely to have NYHA class III to IV symptoms, 79 (42.7%) compared to 182 (30.9%) in control group (p<0.0001). Results of univariable and multivariable analysis is given in table 2. Pre-operative anemia is linked with almost three times increased risk of further renal dysfunction 18.3% vs 6.4% (p<0.0001). patients with anemia also

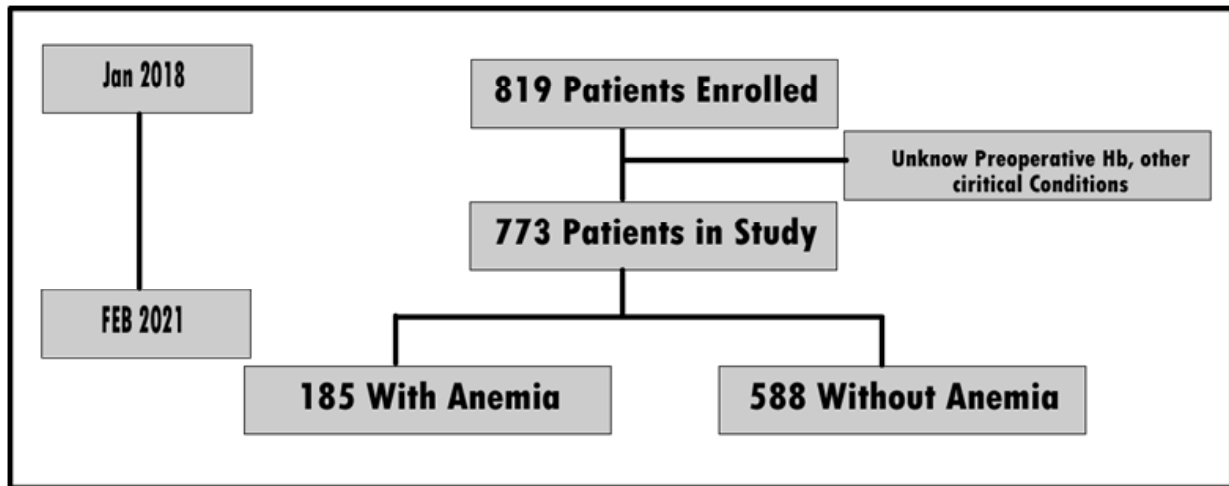


Figure -1: Study Profile

Table -1 Preoperative Characteristics			
Parameter	Preoperative Anemia (n=185)	Control Group (n=588)	p
Age (Years +/- SD)	69 +/- 10.6	64.5 +/- 11.6	< 0.0001
Hemoglobin Level (g/dl +/- SD)	11.5 +/- 1.1	14.3 +/- 1.1	< 0.0001
Female n (%)	51 (27.7%)	141 (23.9%)	<0.001
NYHA Class-III and IV n(%)	79 (42.7%)	182 (30.9%)	<0.0001
Diabetes n (%)	42 (22.7%)	70 (11.9%)	<0.0001
Hypertension n (%)	129 (69.7%)	391 (66.4%)	0.002
Chronic Pulmonary Disease n (%)	29 (15.6%)	65 (11%)	<0.0001
Renal Failure n(%)	9 (4.8%)	4 (0.68%)	<0.0001

tend to be more at risk of developing stroke 2% vs 1% (p=0.008). Atrial fibrillation was also slightly more common in anemic group as compared to control group 36.2% vs 32.9% (p=0.003). Preoperatively anemic patients tend to stay longer

in hospital 53.5% vs 35.8% (p<0.0001). Post CABG myocardial infarction was not influenced by the preoperative anemic condition 4(2%) vs 12 (2%) (p=0.93).

Table 2: Clinical Outcomes

	Anemia Group (n=185)	Control Group (n=588)	P
Renal Dysfunction n(%)	34 (18.3%)	38 (6.4%)	< 0.0001
Atrial Fibrillation n (%)	67 (36.2%)	194 (32.9%)	0.003
Stroke n (%)	4 (2%)	6 (1%)	0.008
Myocardial Infarction n (%)	4 (2%)	12 (2%)	0.93
Length of Hospital Stay (> 7 Days)	99 (53.5%)	211 (35.8%)	<0.0001)

**DISCUSSION:**

Our study indicated that preoperative anemia in patients undergoing isolated CABG is a risk factor contributing to postoperative renal dysfunction, stroke and atrial fibrillation. The preoperative anemia however has no effect on post CABG myocardial infarction. The data indicates that the relative risk of increasing the renal dysfunction is increased by almost three times. It has also clearly shown that anemic patients tend to stay in hospital about 20% more than the non-anemic patients, resulting in increased consumption of hospital resources.

This is an established fact that anemia contributes significantly to the cardiovascular diseases in general population.<sup>13,14</sup> ARIC study concluded that after analyzing 14,410 low risk patients in general population, that anemic patients are more prone to develop myocardial infarction, coronary artery disease and death.<sup>13</sup> Several other studies have shown that anemia is a risk factor mortality and morbidity in patients with congestive cardiac failure and ischemic heart disease.<sup>15-18</sup>

Anemia is a common hematological finding in our patients. Almost 1/3rd of the world population is anemic (33%) by WHO standards. Its incidence has been reported in preoperative CABG patients from 20% to 30%.<sup>3-19</sup> In our sample data, 25% of the patients were anemic. Many studies have shown adverse effects associated with preoperative anemia and poor outcome.<sup>19</sup> Wu et al studied in patients over 310,000 and found that even mild degrees of anemia are related to increased 30 days mortality and morbidity after cardiac surgery.<sup>19</sup> The same study also demonstrated that a hematocrit below 39% is linearly related to cardiac events.<sup>19</sup> Kurkuti et al in a large multicenter study with 3500 patients found that preoperative anemia is an independent risk factor for postoperative stroke, acute kidney injury and death.<sup>3</sup> Clandelas et al

found that preoperative hemoglobin < 12 g/dl is correlated to the postoperative complications of neurological injury, renal injury, postoperative bleeding and reoperations.<sup>5</sup> In addition, Kulier et al showed that low preoperative hemoglobin level was not an independent risk factor for early death or major cardiovascular events after CABG, but only renal and cerebrovascular events are related to it.<sup>10</sup> Varying results showed by these studies might be due to the different standards chosen to define anemia. Most of these studies focused on hemoglobin levels between 10 g/dl to 12.5 g/dl. The strength of our study is that we scaled our patients according to the definitions of WHO.

There are two popular risk stratification models commonly used in cardiac surgery. Both of these models, EuroScore-II and STS score, do not take into consideration preoperative hemoglobin level as a contributing risk. This absence in both these models create a controversy as to whether it is really important or not considering preoperative anemia as a risk factor, like other factors as age, renal dysfunction and diabetes are considered. Renaucci et al hold the point of view that prevalence of anemia is quite low in the population we treat, and low hemoglobin is frequently encountered as part of other co-morbidities, that are addressed by these models, therefore hemoglobin level as such is not considered in these risk stratification models.<sup>7</sup> In our sample almost quarter of patients were anemic, this indicates a quite significant population, that cannot be ignored. Additionally, our data indicates that anemia significantly contributes to postoperative renal failure, stroke and atrial fibrillation.

Preoperative anemia, has many physiological consequences, that become more relevant when the patient experiences stress of surgery and cardiopulmonary bypass. Anemic patients have low oxygen carrying capacity and therefore have

tissue hypoxia and organ dysfunction. This may not be evident at macro level but may be there at micro level in cells. During cardiopulmonary bypass priming volume further dilutes the pre-existing low hematocrit resulting in more tissue edema and poor oxygenation. Sometimes the perfusionists add stored blood from the blood bank to the priming volume, to compensate for this, or in early phase of recovery anesthetist may infuse a unit of banked blood to bring the hemoglobin level at an appropriate level. This pathophysiology and addition of blood products are known to influence the postoperative complications of stroke, renal dysfunction and mortality.<sup>7,20,21</sup>

Anemic patients are the biggest consumers of blood products. It has been convincingly shown that blood product infusion, either in the form of cells or whole blood in cardiac surgery has strong influence on mortality and morbidity.<sup>22</sup> Stored blood cells have structural and functional changes that lead to altered aggregability and rigidity of red blood cells. These micro-particles coupled with activated pro-inflammatory molecules, reduced nitric oxide NO and cytokines may result in vasoconstriction of microcirculation thereby significantly affecting cellular perfusion and oxygenation.<sup>22</sup> These mechanisms may be the pathways of organ dysfunction.

Despite this fact that preoperative anemia has deleterious effects on outcomes after CABG, nevertheless this is a correctable condition. At

least physiology can be corrected and therefore avoid the initiation of deleterious pathways. The updated guidelines of Society of Thoracic Surgeons and the Society of Cardiovascular anesthesia recommend blood conservation therapies. Preoperative administration of erythropoietin and iron are now recommended with the objective of increasing the hemoglobin levels (Class IIa, Level of evidence B).<sup>23</sup> It has also been proposed that preoperative blood transfusion may have a role in correcting the iron metabolism and production of the oxidative reactions before surgery.<sup>24</sup> More studies are required to confirm these beneficial effects.

#### LIMITATIONS:

Research was conducted using retrospective analysis of our institutional records. This study does not take into consideration many unmatched residual factors that may have influenced the outcome. Furthermore, we did not take into account the operative details, and minimum level of hematocrit during cardiopulmonary bypass, post-operative ICU management, blood loss and replacement transfusions.

#### CONCLUSIONS:

We conclude that preoperative anemia, hemoglobin level < 13 g/dl in men and <12 g/dl in women, undergoing coronary artery bypass surgery are at an elevated risk of developing postoperative renal dysfunction, stroke and extended hospitalization.

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