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Original article

Predictive Value of Hemoglobin Level and Subclinical Iron Deficiency on Perioperative Morbidity and Mortality in Patients Undergoing Cardiac Surgeries

Mohamed A. Mohamed[a], Nabil A. Khattab[a], Ahmed G. Elsayed[a], Mohamed A. El-Gazzar[b], Yousry R. Hayes[b], Basma M. Hani[c], Medhat A. Khalil[a]

[a] Department of internal medicine, faculty of medicine, Benha university, Benha, Egypt. [b] Department of Cardiothoracic surgery, faculty of medicine, benha university, Benha, Egypt. [c] Department of Public health and Community Medicine, faculty of medicine, benha university, Benha, Egypt.

Correspondence to: Ahmed G. Elsayed, Department of internal medicine, Benha faculty of medicine, Benha University, Egypt.

Email:

aahmm98@gmail.com

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Abstract

Background: There are several dangers and adverse effects associated with red blood cell transfusions, which are often administered after surgery due to anemia. Our aim is to assess the significance of hemoglobin level and subclinical iron insufficiency on perioperative morbidity and mortality in patients having heart surgery. **Patients and Methods:** This study was conducted on 30 patients undergoing different cardiac surgeries during the period from May 1, 2021, and April 30, 2022**. Results:** Negative correlation between hospital length of stay and both hemoglobin and serum iron levels (r = -0.807, p 0.001). Patients who required a blood transfusion, developed an infection, had problems, were admitted to ICU, or died, had substantially lower iron levels than the rest of the patients (p 0.001). those showed statistically significant association between Hb and the occurrence of problems (AUC = 0.994, p 0.001). The sensitivity is 100% and the specificity is 91.3%. Complications are strongly predicted by serum iron levels (AUC = 0.988, p 0.001). ICU admission may be predicted with high accuracy by Hb (AUC = 1.000, p 0.001). The sensitivity and specificity are both one hundred percent at a cut off value of 9. ICU admission can be predicted with a high degree of accuracy by serum iron levels (AUC=1.000, p0.001). The sensitivity and specificity are both one hundred percent at a cutoff value of 80. **Conclusion:** The results of cardiac surgery were worse for patients who had anemia prior to surgery.

Key words: hemoglobin level - predictive value - iron deficiency anemia - perioperative morbidity and mortality in cardiac surgeries

Introduction:

Approximately 24.8% of people on Earth suffer from anemia, which is characterized by hemoglobin (Hb) content of less than 13 g/dl in males and 12 g/dl in women [1], reduced levels of oxygen in the blood are linked to anemia, which is caused by the lack of hemoglobin (Hb). Inadequate tissue oxygen supply may affect organ function unless blood flow is boosted to compensate. [2]

The haem moiety of hemoglobin cannot be synthesized without iron, and iron also plays a crucial role in oxidative metabolism. As a consequence, iron deficiency may directly impact mitochondrial oxidative metabolism and adenosine triphosphate (ATP) generation through effects on the mitochondria themselves, as well as indirectly via anemia and the reduction of oxygen delivery that results from it. [3]

The prevalence of preoperative anemia is estimated to be between 20 and 30 percent using WHO criteria, and it rises with age and the presence of comorbidities. [1]

Iron-deficiency anemia and anemia due to chronic illness are the most prevalent causes of anemia in patients undergoing heart surgery who need preoperative blood transfusions [4]; Anemia is more likely to occur in cardiac surgery patients because of the acute hemodilution caused by cardiopulmonary bypass (CPB), perioperative phlebotomy, and surgical blood loss. [5]

Patients undergoing cardiac surgery are more likely to have a red blood cell (RBC) transfusion if they were anemic before the procedure. Transfusion responses, transfusion-related immunomodulation, viral complications, and other systemic side effects are all possible with allogeneic blood transfusions despite their scarcity and high cost. [6]

Blood transfusion after heart surgery is linked to higher rates of mortality, durations of hospital stays, and overall healthcare expenses, much as preoperative anemia is. Although it is yet unclear how much preoperative anemia and RBC transfusion independently contributes to bad outcomes in cardiac surgery patients, it has been established that the combination of the two significantly increases morbidity and death. [7]

The goals of this study are: (1) to improve pre and postoperative treatment of anemic patients having heart surgery by constructing and implementing an educational program.

Patients and Methods:

Thirty patients undergoing cardiac surgery at Cardiothoracic Surgery Department during the period from May 1, 2021, and

April 30, 2022**,** were included in this observational cross section study to evaluate the impact of different hemoglobin levels on perioperative morbidity and mortality.

Inclusion criteria: Patients were selected to be between the age of 18 and 60, who have heart lesions, both genders.

Exclusion criteria: BMI of 40 or above, hemolytic anemia, Liver and renal disorders, other chronic diseases, Spent more than 48 hours in the intensive care unit before surgery.

Taking a complete history, including the patient's: personal details (name, age, sex), the nature of the complaint being presented, all important illnesses from infancy, rheumatic fever history, and risk factor for cardiovascular disease, any medical condition or past hospital admission, and the medical history of pharmaceuticals used (perioperative) are all included while compiling a patient's medical history.

Clinical examination included: (1) General assessment of the patient's level of consciousness and mental health, vital data inform of (BP, temperature, heart rate, respiration rate) and there are no indicators of (Pallor, Cyanosis, Jaundice, and Lymph node enlargement), Leg swelling (or edema). (2) Physical examination of: Cardiovascular System, Respiratory System, Gastrointestinal Tract, Central nervous system and motor power.

Investigations during presentations: CBC, Serum creatinine, blood urea, urine sample analysis, AST, ALT, Albumin, Bilirubin, Prothrombin Time, International Normalized Ratio, Serum Gamma-Glutamyl Transferase (GGT), Total lipids, serum total cholesterol, serum HDL cholesterol, serum triglycerides, LDL, Iron levels, Blood sugar levels at random, HbA1c, Echocardiography, were reported.

The patient was monitored during heart surgery and for days 3, 5, 8, 15, and 30, and thereafter to check for complications that required intensive care unit admission, blood transfusions, infections, and duration of hospital stay.

We obtained approval from the institutional research ethics committee and all participants provided written informed permission.

Results:

The cause of cardiac surgery was CABG in 13 (43%) patients, valve replacement in 13 (43%) patients, VSD in 3 (10%) patients, and ASD in 1 (3%) patient **Table 1**.

Regarding laboratory measurements in the study participants, Hb ranged from 7 to 16 g/dL with a mean value of 12.23 ± 309 g/dL, iron ranged from 29 to 170 µg/dL

with a mean value of 100.83 ± 40.52 µg/dL, RBG ranged from 75 to 240 mg/dL with a mean value of 126.97 ± 45.57 mg/dL, HbA1c ranged from 4.8 to 9 % with a mean value of 5.95 ± 1.39 %, urea ranged from 18 to 43 mg/dL with a mean value of 30.33 ± 7.07 mg/dL, creatinine ranged from 0.6 to 1.2 with a mean value of 0.93 ± 0.13 mg/dL, AST ranged from 10 to 35 with a mean value of 21.06 ± 7.49, and ALT ranged from10 to 45 with a mean value of 27.83 ± 8.64 **Table 2**.

Regarding clinical outcomes in the study participants, 9 (30%) patients needed blood transfusion, 7 (23.33%) patients had infection, and 7 (23.33%) patients had complications **Table 3**.

Regarding hospital outcomes in the study participants, 9 (30%) patients needed ICU admission, 6 (20%) patients died in the hospital. The hospital length of stay ranged from 3 to 11 days with a mean value 6.16 ± 2.36 days **Table 4**.

There was a significant negative correlation between hospital length of stay and hemoglobin level (r =-0.807, p <0.001), and serum iron level (r =-0.789, p <0.001) **Table 5.**

Hemoglobin level was significantly lower in patients who had blood transfusion, infection, complications, ICU admission and mortality than the rest of patients (p <0.001) **Table 6.**

Hb is a significant predictor of complications (AUC: 0.994, p value <0.001). At a cut off value of ≤9 it has a sensitivity of 100% and a specificity of 91.3%. Serum iron is a significant predictor of complications (AUC: 0.988, p value <0.001). At a cut off value of ≤80 it has a sensitivity of 100% and a specificity of 91.3% **Table 7**.

Table 1: Causes of cardiac surgery in the study participants

		Study participants (n =30)
Causes of cardiac surgery	**CABG**	13 (43%)
	Valve replacement	13 (43%)
	VSD	3 (10%)
	ASD	1 (3%)

CABG: Coronary artery bypass graft, VSD: Ventricular septal defect, ASD: Arterial septal defect.

Table 2: Laboratory measurements in the study participants

		Study participants (n =30)
Hb (g/dL)	**Mean ± SD**	12.23 ± 3.09
	Range	7 – 16
Iron (µg/dL)	**Mean ± SD**	100.83 ± 40.52
	Range	29 – 170
RBG (mg/dL)	**Mean ± SD**	126.97 ± 45.57
	Range	75 – 240
HbA1c (%)	**Mean ± SD**	5.95 ± 1.39
	Range	4.8 – 9
Urea (mg/dL)	**Mean ± SD**	30.33 ± 7.07
	Range	18 – 43
Creatinine (mg/dL)	**Mean ± SD**	0.93 ± 0.13
	Range	0.6 – 1.2
AST (units/L)	**Mean ± SD**	21.06 ± 7.49
	Range	10 – 35
ALT (units/L)	**Mean ± SD**	27.83 ± 8.64
	Range	10 – 45

Hb: Hemoglobin, RBG: Random blood glucose, AST: Aspartate transaminase, ALT: Alanine transaminase**.**

Table 3: Clinical outcomes in the study participants

		Study participants (n =30)
Need for blood transfusion	**Yes**	9 (30%)
	No	21 (70%)
Infection	**Yes**	7 (23.33%)
	No	23 (76.67%)

Table 4: Hospital outcomes in the study participants

		Study participants (n =30)
Need of ICU admission	**Yes**	9 (30%)
	No	21 (70%)
In hospital mortality	**Yes**	6 (20%)
	No	24 (80%)
Hospital length of stay (days)	**Mean ± SD**	6.16 ± 2.36
	Range	3 – 11

ICU: Intensive care unit

Table 5: Correlation between hemoglobin level and in the study participants

	Hospital length of stay (days)	
	r	**P value**
Hb level (g/dL)	-0.807	**<0.001***
Iron (µg/dL)	-0.789	**<0.001***

Table 6: Relationship between hemoglobin level and outcomes in the study participants

		Hb level (g/dL)	P value
Need for blood transfusion	**Yes**	7.77 ± 0.97	**<0.001***
	No	14.14 ± 0.85	
Infection	**Yes**	7.42 ± 0.78	**<0.001***
	No	13.69 ± 1.69	
Complications	**Yes**	7.43 ± 0.79	**<0.001***
	No	13.69 ± 1.69	
Need of ICU admission	**Yes**	7.78 ± 0.97	**<0.001***
	No	14.14 ± 0.85	
In hospital mortality	**Yes**	7.16 ± 0.41	**<0.001***
	No	13.5 ± 1.91	

*Statistically significant as p value ≤0.05

Table 7: Accuracy of hemoglobin level and serum iron for the prediction of complications

	Cut-off value	Sensitivity	Specificity	AUC	P value
Hb (g/dL)	≤9	100%	91.3%	0.994	**<0.001***
Iron (µg/dL)	≤80	100%	91.3%	0.988	**<0.001***

Hb: Hemoglobin, *statistically significant as p ≤0.05

Discussion:

The types of cardiac surgery performed in this research were CABG on 13 patients (43%), valve replacement on 13 patients (43%), VSD on 3 patients (10%), and ASD on 1 patient (3%).

Participants' hemoglobin levels ranged from 7 to 16 g/dL, with a mean of 12.23 309 g/dL, while their iron levels varied from 29 to 170 g/dL, with a mean of 100.83 40.52 g/dL in this research**.**

Preoperative hemoglobin concentrations ranged from 5.8 to 18.0 g/dL, with a mean (SD) of 13.4 g/dL. The overall prevalence of anemia, defined as hemoglobin concentration <12.5 g/dL, was 26%, with

values ranging from 22% to 30% at the participating hospitals. [8]

Some authors conducted a retrospective study including over 500,000 patients and showed that anemia was linked to higher death within 30 days. [9]

Patients having cardiac and non-cardiac surgery who have abnormal preoperative hemoglobin (Hb) concentrations have a higher risk of complications and death during the perioperative period. There is a significant incidence of anemia, and there is mounting evidence that the transfusion of red blood cells to treat anemia increases the risk of complications after surgery. Furthermore, preoperative augmentation of Hb concentration with iron or erythropoietin replacement is less expensive than treating anemia on an acute basis with red blood cell transfusion. [10]

We discovered that 9 patients (30%) required a blood transfusion, 7 patients (23.33%) had infection and 7 patients (23.33%) experienced problems as a result of the treatment they received in the present research**.**

Nine patients (30%) in the research required intensive care unit hospitalization, and six patients (20%) passed away while hospitalized. Inpatient stays averaged 6.16 days (SD 2.36 days) but varied widely between 3 and 11 days. ICU admission rates for patients with preoperative anemia were higher than those for those with normal preoperative Hb values. Patients with severe anemia had a higher rate of ICU admission after surgery. For every level of preoperative Hb concentration, males were admitted to ICU at a higher rate than women**.**

Non-cardiac patients with abnormal preoperative Hb values have been shown to have an elevated risk of death in many retrospective investigations. [11]

Researchers found that individuals with preoperative anemia or polycythemia had a higher risk of death and cardiac events in the first 30 days after surgery. [11]

Authors conducted another large retrospective cohort analysis, this time looking at data from over 200,000 patients who had significant non-cardiac surgery, show that preoperative anemia is related with an elevated risk of morbidity and death in these patients for up to 30 days after surgery. There was no difference in the adverse effects of preoperative anemia based on age or gender**.** [12]

In addition to the above, we also discovered a negative link between the amount of time a patient spent in the hospital and their hemoglobin and serum iron levels ($r = -0.807$, p 0.001, and $r = -0.789$, p 0.001, respectively).

The median duration of stay decreased by half a day for every unit rise in admission hemoglobin level. The median duration of stay increased by 1.5 days for every unit of hemoglobin variation**.** [13]

The present research showed that individuals who had a blood transfusion, had an infection, experienced difficulties, were admitted to the intensive care unit, or died, had a considerably lower hemoglobin level than the other patients. Patients who required a blood transfusion, developed an infection, had problems, were admitted to the intensive care unit (ICU), or died had substantially lower iron levels than the rest of the patients (p 0.001).

Our own research also shows that Hb is a robust predictor of problems (AUC=0.994, p0.001). The sensitivity is 100% and the specificity is 91.3% at a cut off value of 9. Complications are strongly predicted by serum iron levels (AUC = 0.988, p 0.001). It has a cutoff value of 80, at which point it is 100% sensitive and 91.3% specific. In addition, Hb is an excellent predictor of admission to the intensive care unit (AUC = 1.000, p 0.001). The sensitivity and specificity are both one hundred percent at a cut off value of 9. ICU admission may be predicted with a high degree of accuracy by serum iron levels (AUC=1.000, p0.001). The sensitivity and specificity are both one hundred percent at a cutoff value of 80**.**

Anemia before surgery was linked to an increased risk of developing both new renal failure and multisystem failure. [14]

Patients whose preoperative hemoglobin concentration was 10 g/dl or fewer had a threefold increased risk of in-hospital mortality after CABG. [15]

Finally observed that, in the context of cardiac valve surgery, patients with preoperative hemoglobin 12 mg/dl had a 3-fold increased risk of death and 5-fold in the Odds of developing major postoperative complications like heart failure, myocardial infarction, reoperation for bleeding, neurological complication and acute renal failure. [16]

Low preoperative hemoglobin level was not an independent risk factor for early death after CABG and it was only marginally relevant for morbidity even in elderly patients. [17]

Iron concentration 6 mol/l was the best cutoff point for predicting hospitalization. In this range, iron levels were 94.7% sensitive and 67.9% specific. Area under the ROC curve (AUC) measures the ability to predict outcomes and iron's AUC was 0.894 with a 95% confidence range of 0.858-0.931. TfSat, transferrin, ferritin, and CRP all had smaller area under the receiver operating characteristic (AUC) curves compared to iron (0.863 (CI 0.824-0.903),

0.735 (CI 0.676-0.795), 0.725 (CI 0.667-0.784), and 0.838 (CI 0.790-0.886), respectively). [18]

Our findings imply that routine monitoring of serum iron levels in outpatients may help in the early detection of worsening**.**

Limitation of the study:

This study is limited by the number of patients included and the follow-up period. Additionally, the study is a single-center experience.

Conclusion:

As this study's findings show, preoperative anemia is independently linked to poor outcomes after heart surgery. It's important to note that the effects of RBC transfusion had no role in this correlation. Preoperative anemia, with a hemoglobin level of 13 g/dl for men and 12 g/dl for women, is an independent risk factor for death, postoperative renal dysfunction, stroke, and longer hospital stay in patients having heart surgery. Patients having heart surgery may benefit from therapy targeted at reducing their anemia before the procedure

References:

1- **Organization, W.H.** "Hemoglobin concentrations for the diagnosis of anemia and assessment of severity. Vitamin and Mineral Nutrition Information System. 2011. Geneva", World Health Organization (WHO/NMH/NHD/MNM/11.1). Available from: Http://www.Who.Int/Vmnis/Indicators/Haemoglobin.

2- **Sanders J, Cooper JA, Farrar D, Braithwaite S, Sandhu U, Mythen M, et al.** Pre-operative anaemia is associated with total morbidity burden on days 3 and 5 after cardiac surgery: a cohort study. Perioperative Medicine. 2017;6(1):1-2.

3- **Paul BT, Manz DH, Torti FM, Torti SV.** Mitochondria and Iron: current questions. Expert review of hematology. 2017;10(1):65-79.

4- **Nguyen Q, Meng E, Berube J, Bergstrom R, Lam W.** Preoperative anemia and transfusion in cardiac surgery: a single-centre retrospective study. Journal of Cardiothoracic Surgery. 2021;16(1):1-8.

5- **Dai L, Mick S, McCrae K, Houghtaling P, Sabik J, Blackstone E, et al.** Preoperative anemia in cardiac operation: does hemoglobin tell the whole story?. The Annals of thoracic surgery. 2018;105(1):7-100.

6- **LaPar D, Hawkins R, McMurry T, Isbell J, Rich J, Speir A, et al.** Preoperative anemia versus blood transfusion: which is the culprit for worse outcomes in cardiac surgery?. The Journal of thoracic and cardiovascular surgery. 2018;156(1):66-74.

7- **Padmanabhan H, Brookes MJ, Nevill AM, Luckraz H.** Association between anemia and blood transfusion with long-term mortality after cardiac surgery. The Annals of Thoracic Surgery. 2019;108(3): 92-687.

8- **Karkouti K, Duminda N and Wijeysundera W. (2008):** Risk Associated With Preoperative Anemia in Cardiac Surgery, A Multicenter Cohort Study Scott

Beattie and for the Reducing Bleeding in Cardiac Surgery (RBC) Investigators.

9- **Saager L, Turan A, Reynolds L, Dalton J, Mascha E, Kurz A. (2013**): The association between preoperative anemia and 30-day mortality and morbidity in noncardiac surgical patients, Anesth Analg, 117, pp. 909-915.

10- **Karkouti K, Stukel T, Beattie W, Elsaadany S, Li P, Berger R, et al., (2012):** Relationship of erythrocyte transfusion with short- and long-term mortality in a population-based surgical cohort, Anesthesiology, 117, pp. 1175-1183.

11- **Wu W, Schifftner T, Henderson W, Eaton C, Poses R, Uttley G, et al, (2007**). Preoperative hematocrit levels and postoperative outcomes in older patients undergoing noncardiac surgery, J Am Med Assoc, 297, pp. 2481-2488.

12- **Musallam K, Tamim H, Richards T, Spahn D, Rosendaal F, Habbal A, et al. (2011):** Preoperative anemia and postoperative outcomes in non-cardiac surgery: a retrospective cohort study, Lancet, 378, pp. 1396-1407.

13- **Lin R, Evans A, Chused A, Unterbrink ME. (2013).** Anemia in general medical inpatients prolongs length of stay and increases 30-day unplanned readmission rate. *Southern medical journal*, *106*(5), 316–320.

14- **Al-Riyami A, Baskaran B, Panchatcharam SM, Al-Sabti H. (2021):** Preoperative Anemia is Associated with Increased Intraoperative Mortality in Patients Undergoing Cardiac Surgery. Oman Med J;36(3):e267.

15- **Zindrou D, Taylor K and Bagger J. (2002):** Preoperative hemoglobin concentration and mortality rate after coronary artery bypass surgery. Lancet;359(9319):1747-1748.

16- **Cladellas M, Bruguera J, Comín J, Vila J, Jaime E, Martí J, et al.** Is pre-operative anaemia a risk marker for in-hospital mortality and morbidity after valve replacement?. European heart journal. 2006;27(9):1080-1093.

17- **Bell M, Grunwald G, Baltz J, McDonald G, Bell M, Grover F, et al. (2008):** Does preoperative hemoglobin independently predict short-term outcomes after coronary artery bypass graft surgery? Ann Thorac Surg. Nov;86(5):1415-1423.

18- **Hippchen T, Altamura S, Muckenthaler MU, Merle U. (2020).** Hypoferremia is Associated With Increased Hospitalization and Oxygen Demand in COVID-19 Patients. *HemaSphere*, *4*(6), e492.

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