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Original Article

Pre-operative Anemia as a Risk Factor of Morbidity and Mortality in Valvular Surgeries

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ABSTRACT

Pre-operative anemia can be a hindrance to speedy recovery and will increase blood transfusion intraoperative and post operatively. **Objective:** To find a correlation between preoperative anemia and the subsequent morbidity and mortality rates in patients undergoing valvular surgeries. **Methods:** A retrospective observational study, involving 493 valvular surgeries' patients. All patients had the same anesthetic and surgical techniques. According to the WHO, anemia is a hemoglobin level < 13 g/dl for men and <12 g/dl for women. Clinical variables were compared using chi-square and independent t-test. **Results:** The patients received cardiac surgery for valvular heart disorders and had an average age of 42.2±14.1 years, with 60.9% being male. Most patients exhibited NYHA III (48.9%) and CCS III (36.5%) functional class symptoms. Highest comorbidity was hypertension (35.1%), followed by diabetes (14.4%) and dyslipidemia (6.5%). 43.2% were anemic and older than non-anemic individuals (P=0.02). Anemic people had a significantly greater incidence of HTN (P 0.02) and DM (P < 0.001). Both groups exhibited identical perfusion and cross-clamp periods (P=0.4 vs. P=0.3). Though not statistically significant (P=0.08), non-anemic patients needed more intraoperative blood or blood product transfusions. Patients with anemia have worse outcomes, including increased rates of in-hospital mortality (P=0.03), extended artificial breathing (P=0.04), and postoperative blood/product transfusion (P<0.001). 44.8% of anemic individuals needed RCC, 41.9% FFP, and 41.4% platelets. **Conclusions:** anemia is associated with the poorest post-operative results. There is conflicting information about the impact of preoperative anemia, particularly iron deficiency anemia, on valvular surgery.

INTRODUCTION

Anemia is characterized by a deficiency in the number of red blood cells or the hemoglobin concentration in the blood, resulting in reduced oxygen-carrying capacity. It is defined by the World Health Organization as a hemoglobin level of less than 13 g/dl for males and less than 12 g/dl for females [1]. This condition can arise from various factors, including nutritional deficiencies (such as iron, vitamin B12, or folate), chronic diseases (such as renal insufficiency or inflammatory conditions), or genetic disorders affecting red blood cell production or lifespan. Anemia manifests clinically with symptoms such as fatigue, weakness, shortness of breath, and pallor, reflecting the diminished oxygen delivery to tissues throughout the body. Anemia is a recognized risk factor that contributes negatively to cardiovascular health [2]. In the specific context of valvular surgeries, preoperative anemia represents a significant risk factor that warrants careful consideration in the perioperative management of patients [3]. Decreased hemoglobin levels imposed by valvular dysfunction exacerbate the deleterious effects of anemia, mainly associated with higher rates of death and morbidity in the elderly, those with heart failure, and people with ischemic

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heart diseases, especially when acute coronary syndrome is present, as shown by multiple research studies [4,5]. Nonetheless, the impact of preoperative anemia in cardiac surgery remains a topic of debate. Earlier studies have identified preoperative anemia as a distinct risk factor for in-hospital mortality and adverse outcomes following valve surgery [6-8]. Moreover, the inflammatory response elicited by surgical trauma further exacerbates the anemia-related oxygen deficit, amplifying the risk of ischemic events and organ dysfunction [9,10]. Anemia's effects on the cardiovascular system are not the only ones that come after valve surgery. It increases the risk of post-operative problems, lengthens hospital stays, and increases the need for blood transfusions in patients receiving valvular operations [11]. Anemia impedes the flow of oxygen to tissues, which exacerbates these negative consequences and leads to higher rates of morbidity and death. [12].

The objective of our study was to predict morbidity and mortality in patients undergoing valvular heart surgeries through preoperative anemia analysis in our set up.

METHODS

A retrospective observational study was conducted at Rehman Medical Institute, Peshawar, between 2018 and 2023, involving patients who underwent valvular surgeries. The study included a sample of approximately 495 patients and collected detailed clinical data, amongst which 280 were anemic and 215 were non-anemic. Exclusion criteria comprised individuals with unknown preoperative hemoglobin levels and those who met any of the following criteria before surgery: ventricular tachycardia or fibrillation or survived sudden cardiac arrest, required preoperative cardiac resuscitation, needed preoperative mechanical ventilation prior to entering the anesthesia room, received preoperative inotropic support, underwent intra-aortic balloon pump, or experienced preoperative acute renal failure (characterized by anuria or oliguria of less than 10 ml/hour) or required emergency surgery. Uniform anesthetic and surgical procedures were applied to all patients. Following the conclusion of the surgery, patients were transferred to the intensive care unit and received care in accordance with the unit's established protocol. After approval by Ethical Review Board of Rehman Medical institute (RMI/RMI-REC/Article Approval / 102), data collection was started by taking informed consent from all the subjects involved in the study. The data collection tool used was Questionnaire to be filled by trained doctors. Study population was divided into two groups (anemic and non-anemic). Data were analyzed using SPSS version 26.0. Mean±SD were presented for quantitative variables like age, weight and hemoglobin level. Frequency and percentages were computed for qualitative variables like gender. The differences in the mean hemoglobin level of both groups were statistically tested using the student t test, p ≤0.05 was considered statistically significant. The primary outcome was considered as In-hospital Mortality while Prolonged hospital stay was taken as secondary outcome.

RESULTS

The study comprised 493 patients with a mean age of 42.2±14.1 who underwent cardiac operations for valvular heart disorders, with 60.9% being men. The majority of patients exhibited NYHA III symptoms (48.9%) and CCS III functional class symptoms (36.5%). The most common comorbidity was hypertension (35.1%), followed by diabetes mellitus (14.4%) and dyslipidemia (6.5%). The average hematocrit level before surgery was 36.4±11.4 (table 1). Out of the 493 patients, 43.2% had Anemia, and their average age was 43.7±15.7. Anemic patients were older than non-anemic patients (P=0.02), although the latter had a slightly higher percentage of male population (32.5%) (P=0.06). Anemic patients showed a higher likelihood of having hypertension (P 0.02) and diabetes (P <0.001) compared to non-anemic patients, who were more likely to have a similar history of myocardial infarction (P 0.4). Anemic individuals were more likely to have a history of dyslipidemia (P=0.2), cerebrovascular accident (P=0.3), previous PCI (P=0.08), and family history of CAD (P=0.1), but these associations were not statistically significant. Both groups had similar presenting complaints, although the majority of non-anemic patients exhibited NYHA III functional class symptoms. Most anemic patients had reduced LVEF<50%, while the majority of non-anemic patients had maintained LVEF>50%. There was no notable disparity between the two groups regarding tobacco smoking, family history of CAD, dyslipidemia, CVA, MI, and PCI (table 1).

Table 1: Pre-Operative Patients' Parameters

Sr. No	Parameters	Anemic=213	Non-Anemic = 280	p-value
1	Age (Mean)	43.7±15.7	40.7±13.6	0.02
2	Male	140 (28.4%)	160 (32.5%)	0.06
3	Female	73 (14.8%)	120 (24.3%)	
4	Tobacco Used	16 (3.2%)	26 (5.3%)	0.5
5	Current Tobacco	2 (0.4%)	8 (1.6%)	0.1
6	CAD+	8 (1.6%)	4 (0.8%)	0.1
7	Diabetes	47 (9.5%)	24 (4.9%)	<0.001
8	Dyslipidemia	17 (3.4%)	15 (3.0%)	0.2
9	Hematocrit (mean)	27.7±12	44±4.186	<0.001
10	HTN	87 (17.6%)	(17.4%)	0.02
11	Cerebrovascular	6 (1.3%)	4 (0.9%)	0.3
12	PCI	5 (1.0%)	1 (0.2%)	0.08
13	MI	6 (1.2%)	12 (2.4%)	0.4
14	NYHA I	10 (2.0%)	13 (2.6%)	1.0
15	NHYA II	40 (8.1%)	67 (13.6%)	0.1

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16	NYHA III	112 (22.7%)	129 (26.2%)	0.1
17	NYHA IV	21 (4.3%)	23 (4.7%)	0.5
18	CCS I	14 (2.8%)	21 (4.3%)	0.7
19	CCS II	49 (9.9%)	75 (15.2%)	0.3
20	CCS III	82 (16.6%)	98 (19.9%)	0.4
21	CCS IV	30 (6.1%)	29 (5.9%)	0.2
22	EF < 50%	49 (10.0%)	39 (7.9%)	0.4
23	EF > 50%	163 (33.2%)	240 (48.9%)	0.6

There was no significant difference in perfusion and cross-clamp time between the two groups based on intraoperative parameters (P=0.4 vs. P=0.3). The rate of IABP insertion was comparable between the two groups (P=1.0). Non-anemic patients required a higher rate of intraoperative blood/product transfusion compared to anemic patients. However, the difference was not statistically significant (P=0.08) as shown in table 2.

Table 2: Intra-Operative Patients' Parameters

Sr. No	Parameters	Anemic=213	Non-Anemic=280	p-value
1	IABP	3 (0.6%)	3 (0.6%)	1.0
2	Intra-op Blood/ product Transfusion	121 (24.5%)	136 (27.6%)	0.08
3	Perfusion Time (Mins)	111±45.9	108.2±45	0.4
4	X-Clamp Time (Mins)	75.9±32.4	73.5±33	0.3

Anemic patients have the poorest results, including a notably higher in-hospital death rate (P=0.03), prolonged initial mechanical breathing (P=0.04), and an increased need for postoperative blood/product transfusions (P<0.001). 44.8% of anemic patients needed red cell concentrate (RCC), 41.9% needed fresh frozen plasma (FFP), and 41.4% needed platelet transfusion. There was no significant statistical difference in the need for FFP and platelet transfusions across the groups, but non-anemic individuals required significantly more RCC transfusions (P=0.002). There are no significant differences in prolonged breathing, reintubation, return to the ICU, and reopening for bleeding/tamponade (table 3).

Table 3: Post-Operative Patients' Parameters

Sr. No	Parameters	Anemic=213	Non-Anemic=280	p-value
1	Post-op Blood/ Product Transfusion	111 (22.5%)	93 (18.9%)	<0.001
2	RBC Unit	156 (44.8%)	192 (55.2%)	0.002
3	FFP Unit	112 (41.9%)	169 (58.1%)	0.07
4	Platelet Unit	121 (41.4%)	171 (58.6%)	0.5
5	Mean Mechanical Ventilation (hours)	9.59±13.0	7.58±9	0.04
6	Re-admitted ICU	4 (0.8%)	1 (0.2%)	0.1
7	Re-intubated	6 (1.2%)	12 (2.4%)	0.4
8	Re-opened	13 (2.6%)	16 (3.2%)	0.8
9	Post-op Stroke	3 (0.6%)	8 (1.6%)	0.3
10	Prolong Vent	7 (1.4%)	10 (2.0%)	1.0
11	Cardiac Arrest	3 (0.6%)	1 (0.2%)	0.3
12	AF	6 (1.2%)	14 (2.8%)	0.2
13	In Hospital Mortality	16 (3.2%)	9 (1.8%)	0.03

DISCUSSION

According to the current study, pre-operative anemia in patients having valvular surgery is a reliable indicator of death and morbidity. Beyond the immediate consequences of preoperative anemia, patients with anemia had a lower 1-year survival rate than patients without anemia, according to the research by Von Heymann *et al.* The results of a prior trial with 3131 individuals having heart surgery, for which a 3-year follow-up was available, indicate that this impact could persist even longer [13]. The study by Wu *et al.*, demonstrated the impact of preoperative hematocrit levels in older patients undergoing non-heart surgery and found that there may be a 30-day increase in hospital stays, unfavorable outcomes, and mortality. Moreover, a hematocrit level below 39% was closely correlated with cardiac events and mortality [14]. These studies mentioned have strong correlation with our study in terms of outcomes. Additionally, preoperative Anemia may compensate for renal impairment and other additional risk factors. Anemia may be induced or result from renal dysfunction. [16,17]. Another research by Karkouti *et al.*, found the previously reported connection between pre-operative anemia and increased hospital stay, morbidity, and mortality. [15]. According to literature report, it was shown that pre-operative hemoglobin levels below 12 g/dL were a credible indication of mortality within the hospital setting (odds ratio, 3.23; 95% confidence interval, 1.09-9.55; p-value = 0.03) [13]. Even after taking into account EuroScore, pre-operative HB was of considerable importance (odds ratio, 3.64; 95% confidence interval, 1.32-10.06; P = 0.01). The same model was used to forecast post-operative morbidity, and it was discovered that pre-operative hemoglobin levels below 12 g/dL were an independent predictor (odds ratio, 4.67; 95% confidence interval, 2.03-10.71; P < 0.001) and (odds ratio, 5.18; 95% confidence interval, 2.18-12.3; P < 0.001), regardless of whether EuroScore was included or not. CPB is frequently used for valve procedures. It has a number of negative effects, including hemodilution, blood loss, and hemolysis; in anemic people, these effects are more severe. The primary factor influencing peri-operative red blood cell infusions is preoperative anemia. [18]. Blood transfusion has been found to be a distinct feature that can predict unfavorable outcomes and mortality following heart surgery, along with worse long-term outcomes for patients and higher costs. [19-21]. Allogenic blood can restore hemoglobin levels, however when stored red blood cells are first transfused, their oxygen-carrying capability is reduced. Additionally, our analysis revealed a greater (P<0.001) rate of postoperative blood and product transfusions. Of the patients who were anemic, 44.8% needed RCC, 41.9% needed FFP, and 41.4% needed platelet

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transfusion.

CONCLUSIONS

Keeping in view the conditions mentioned above, anemia is linked with the worst post-operative outcomes and is considered major risk factor for increase mortality and morbidity. But there is ambiguous information regarding the effect of particularly anemia or other types of preoperative anemia on valvular surgery.

Authors Contribution

Conceptualization: SSA, MUI
Methodology: SSA, MWS
Formal analysis: SSA, AS, IK, SNS
Writing-review and editing: SSA, MWS, HN, RA, OI, UA,

All authors have read and agreed to the published version of the manuscript.

Conflicts of Interest

The authors declare no conflict of interest.

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REFERENCES

[1] Maakaron JE, Taher AT, Conrad ME. Anemia. 2023. [Last cited: 1st March 2024]. Available at: https://emedicine.medscape.com/article/198475-overview?form=fpf.

[2] Johnson RL and Rubenstein SD. Anemia in the emergency department: evaluation and treatment. Emergency Medicine Practice. 2013 Nov; 15(11): 1-5.

[3] Vos T, Allen C, Arora M, Barber RM, Bhutta ZA, Brown *et al.* Global, regional, and national incidence, prevalence, and years lived with disability for 310 diseases and injuries, 1990–2015: a systematic analysis for the Global Burden of Disease Study 2015. The Lancet. 2016 Oct; 388(10053): 1545-602.

[4] Peyrin-Biroulet L, Williet N, Cacoub P. Guidelines on the diagnosis and treatment of iron deficiency across indications: a systematic review. The American Journal of Clinical Nutrition. 2015 Dec; 102(6): 1585-94. doi: 10.3945/ajcn.114.103366.

[5] Global News Wire. Anemia Treatment Drugs: 2019 Global Market Study; Analyzed by Type of Anemia, Type of Drug, and Geography. 2019. [Last Cited: 1st march 2024]. Available at: https://www.globenewswire.com/news-release/2019/04/26/1810348/0/en/Anemia-Treatment-Drugs-2019-Global-Market-Study-Analyzed-by-Type-of-Anemia-Type-of-Drug-and-Geography.html

[6] Nappi J. Anemia in patients with coronary artery disease. American Journal of Health-System Pharmacy. 2003 Jul; 60(suppl_3): S4-8. doi: 10.1093/ajhp/60.suppl_3.S4.

[7] Carson JL, Duff A, Poses RM, Berlin JA, Spence RK, Trout R *et al.* Effect of anaemia and cardiovascular disease on surgical mortality and morbidity. The Lancet. 1996 Oct; 348(9034): 1055-60. doi: 10.1016/S0140-6736(96)04330-9.

[8] van Straten AH, Külcü K, Özdemir HI, Elenbaas TW, Hamad MA. Preoperative hemoglobin level as a predictor of mortality after aortic valve replacement. Journal of Cardiothoracic and Vascular Anesthesia. 2013 Aug; 27(4): 716-22. doi: 10.1053/j.jvca.2012.12.021.

[9] Elmistekawy E, Rubens F, Hudson C, McDonald B, Ruel M, Lam K, *et al.* Preoperative anaemia is a risk factor for mortality and morbidity following aortic valve surgery. European Journal of Cardio-Thoracic Surgery. 2013 Dec; 44(6): 1051-6. doi: 10.1093/ejcts/ezt143.

[10] Vincentelli A, Susen S, Le Tourneau T, Six I, Fabre O, Juthier F *et al.* Acquired von Willebrand syndrome in aortic stenosis. New England Journal of Medicine. 2003 Jul; 349(4): 343-9. doi: 10.1056/NEJMoa022831.

[11] De Backer O, Arnous S, Lønborg J, Brooks M, Biasco L, Jönsson A *et al.* Recovery from anemia in patients with severe aortic stenosis undergoing transcatheter aortic valve implantation–prevalence, predictors and clinical outcome. PloS One. 2014 Dec; 9(12): e114038. doi: 10.1371/journal.pone.0114038.

[12] Hogervorst EK, Rosseel PM, van de Watering LM, Brand A, Bentala M, van der Bom JG *et al.* Intraoperative anemia and single red blood cell transfusion during cardiac surgery: an assessment of postoperative outcome including patients refusing blood transfusion. Journal of Cardiothoracic and Vascular Anesthesia. 2016 Apr; 30(2): 363-72. doi: 10.1053/j.jvca.2015.10.021.

[13] Von Heymann C, Kaufner L, Sander M, Spies C, Schmidt K, Gombotz H *et al.* Does the severity of preoperative anemia or blood transfusion have a stronger impact on long-term survival after cardiac surgery? The Journal of Thoracic and Cardiovascular Surgery. 2016 Nov; 152(5): 1412-20. doi: 10.1016/j.jtcvs.2016.06.010.

[14] Wu WC, Schifftner TL, Henderson WG, Eaton CB, Poses RM, Uttley G *et al.* Preoperative hematocrit levels and postoperative outcomes in older patients undergoing noncardiac surgery. JAMA. 2007 Jun; 297(22): 2481-8. doi: 10.1001/jama.297.22.2481.

[15] Karkouti K, Wijeysundera DN, Beattie WS. Risk associated with preoperative anemia in cardiac surgery: a multicenter cohort study. Circulation.

DOI: https://doi.org/10.54393/pjhs.v5i03.1269

2008 Jan; 117(4): 478-84. doi: 10.1161/CIRCULATIONAHA.107.718353.

[16] Bell ML, Grunwald GK, Baltz JH, McDonald GO, Bell MR, Grover FL *et al.* Does preoperative hemoglobin independently predict short-term outcomes after coronary artery bypass graft surgery? The Annals of Thoracic Surgery. 2008 Nov; 86(5): 1415-23. doi: 10.1016/j.athoracsur.2008.07.088.

[17] De Santo L, Romano G, Della Corte A, de Simone V, Grimaldi F, Cotrufo M *et al.* Preoperative anemia in patients undergoing coronary artery bypass grafting predicts acute kidney injury. The Journal of Thoracic and Cardiovascular Surgery. 2009 Oct; 138(4): 965-70. doi: 10.1016/j.jtcvs.2009.05.013.

[18] Khanna MP, Hébert PC, Fergusson DA. Review of the clinical practice literature on patient characteristics associated with perioperative allogeneic red blood cell transfusion. Transfusion medicine reviews. 2003 Apr; 17(2): 110-9. doi: 10.1053/tmrv.2003.50008.

[19] Koch CG, Li L, Duncan AI, Mihaljevic T, Loop FD, Starr NJ *et al.* Transfusion in coronary artery bypass grafting is associated with reduced long-term survival. The Annals of Thoracic Surgery. 2006 May; 81(5): 1650-7. doi: 10.1016/j.athoracsur.2005.12.037.

[20] Banbury MK, Brizzio ME, Rajeswaran J, Lytle BW, Blackstone EH. Transfusion increases the risk of postoperative infection after cardiovascular surgery. Journal of the American College of Surgeons. 2006 Jan; 202(1): 131-8. doi: 10.1016/j.jamcollsurg.2005.08.028.

[21] Reeves BC and Murphy GJ. Increased mortality, morbidity, and cost associated with red blood cell transfusion after cardiac surgery. Current Opinion in Anesthesiology. 2008 Oct; 21(5): 669-73. doi: 10.1097/ACO.0b013e32830dd087.