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Impact of Anaemia and Perioperative Transfusion on Mobidity and Mortality in Adult Patients Undergoing Cardiac Surgery: A Prospective Observation Study

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ABSTRACT

Background: Anaemia is highly prevalent among patients undergoing cardiac surgery and is frequently managed with perioperative blood transfusion. However, both anaemia and transfusion have been independently associated with adverse outcomes, including increased morbidity and mortality.

Objective: To evaluate the impact of preoperative anaemia and perioperative blood transfusion on postoperative morbidity and mortality in adult patients undergoing cardiac surgery.

Methods: This prospective observational study included 1100 adult patients undergoing cardiac surgery over a period of 24 months. Patients were stratified based on preoperative haemoglobin levels into anaemic and non-anaemic groups, and further categorized based on perioperative transfusion status. Primary outcomes included 30-day postoperative morbidity and mortality. Secondary outcomes included length of hospital stay and ICU admission.

Results: There were a total number of 439 (39.9%) mitral valve replacements and 93 (8.5%) number of aortic valve replacements performed. Out of all the patients, 412 (37.5%) patients were anaemic with a mean haemoglobin level of 11.5 ± 1.1 g/dl whereas 688 (62.5%) patients were non anaemic with a mean haemoglobin level of 14.4 ± 1.4 g/dl There were a total number of 6253 transfusions with a mean of 5.7 ± 6.1 transfusions per patient. The patients who did not receive any transfusion were 267 (24.3%) in number. There were a total number of 50 (4.5%) deaths during the study. Maximum number of deaths occurred in the group AT (35 deaths, 9.9%) where the patients were anaemic and received perioperative transfusion. The other groups where either one or none of the factors (i.e. anaemia and transfusion) were present had lesser number of deaths [group NT (12 deaths, 1.1%), group AN (1 death, 0.1%), group NN (2 deaths, 0.2%)]. The differences in mortality observed in the 4 groups were statistically significant ($p < 0.001$).

Conclusion: Preoperative anaemia and perioperative transfusion are significantly associated with increased postoperative morbidity and mortality in cardiac surgery patients. Optimization of haemoglobin levels and restrictive transfusion strategies may improve outcomes.

Keywords*: Anaemia, Blood transfusion, Cardiac surgery, Morbidity, Mortality.*

INTRODUCTION:

Anaemia is a condition in which the number of red blood cells or their oxygen-carrying capacity is insufficient to meet the physiological needs of the body. The World Health Organisation (WHO) defines clinical anaemia in adults as haemoglobin concentration of < 13 g/dl in men, < 12 g/dl in non-pregnant women and < 11 g/dl in pregnant women.[1]

Anaemia affects 1.62 billion people around the world, which equals to 24.8% of the population as per the 2008 WHO global database. Even though the highest prevalence (47.4%) is in preschool-age children, the population group with the greatest number of individuals affected is non-pregnant women (468.4 million, 30.2%).[1] In an issue of *Blood*, Kassebaum et al. estimated that the global anaemia prevalence was 32.9% resulting in 68.4 million years lived with disability, which emphasizes the impact of anaemia to the overall global burden of disease.[2]

India continues to be a country with very high prevalence of anaemia in the world because of low overall dietary intake and chronic blood loss due to infections such as malaria and hook worm infestations. A research paper from the *Nutrition Foundation of India* in 2018 found out that the prevalence of anaemia in India ranged between 57.1% and 89.3%, which is much higher than the global standards.[3] As per a recent study from India in 2018, the prevalence of preoperative anaemia in cardiac surgery patients as per the WHO definition was found out to be as high as 51.95%.[4]

There is convincing evidence that the presence of anaemia causes increased morbidity and mortality in both surgical and nonsurgical population. Even mild perioperative anaemia is independently associated with an increased risk of 30 day morbidity and mortality in patients undergoing major non-cardiac surgery.[5] In patients undergoing cardiac surgery with cardiopulmonary bypass (CPB), morbidity, mortality, perioperative acute myocardial infarction and adverse event rates are higher in anaemic patients.[6] In addition, compared with patients without anaemia, the need for airway support, renal replacement therapy and the rate of in-hospital surgical site infection were higher in the anaemic patients.[7] Furthermore, anaemic patients with iron-deficiency had a longer hospital length of stay than patients with sufficient iron stores.[8]

Blood transfusion is associated with several complications that often are serious and contribute to increased morbidity and mortality. Blood transfusion during cardiac surgery increases the risk of low output heart failure[9] respiratory complications, stroke[10], postoperative infections, cost, and increased mortality.[11] The average number of transfusions in cardiac surgery patients is high in spite of various perioperative blood conservation manoeuvres and advanced technologies. Packed red blood cells (PRBC) transfusion is an independent risk factor for increased length of stay in patients undergoing cardiac surgery.[12] Each PRBC unit transfusion is associated with a 29% increase in crude risk of major infections like pneumonia and bloodstream infections.[13] Not only PRBC, but other blood products transfusion also results in increased morbidity and mortality. Cardiac surgery patients receiving platelet transfusion in the operating room to decrease blood loss often required more vasoactive medication, prolonged ventilation and prolonged intensive care.[14] Even in paediatric cardiac surgery patients, fresh frozen plasma and cryoprecipitate transfusion was associated with increased pulmonary complications.[15]

Likewise anaemia and blood transfusion together have been shown to result in worse outcomes, greater than the additive effects of both. Literature at present is not clear on the benefits of restrictive transfusion strategy during adult cardiac surgery. Also, anaemia in patients undergoing cardiac surgery in Indian population has not been well studied. The present study tries to look at the prevalence of anaemia in Indian population and the impact of anaemia and transfusion on perioperative morbidity and mortality in patients undergoing cardiac surgery.

Most cardiac anesthesiologists would agree that it is reasonable to transfuse blood when Hb is <7 g/dL and transfusion is unnecessary when Hb is >10 g/dL. The individualized approach perhaps is needed in a situation in which Hb is between 7.1 g/dL and 9.9 g/dL, and this warrants the development of a multidisciplinary and multimodal transfusion protocol by an institution that should be based on a restrictive strategy.[16]

Prevalence of anaemia is high in Indian population and the number of patients undergoing cardiac surgery is increasing each year. Most of the studies that have reported prevalence of anaemia are from the western population, but Indian literature is scarce on the subject. So Present study was undertaken to correlate anaemia and perioperative transfusion with perioperative morbidity and mortality in cardiac surgery.

MATERIAL & METHODS:

The Present Prospective observational study was conducted in the unit of cardiac anaesthesiology, Department of Anaeasthesiology and Intensive care, G B Pant Institute of Postgraduate Medical Education and Research, New Delhi. Study was conducted January 2018 to july 2019. The study was conducted after approval from the Institutional Ethics Committee. Study includes 1100 adult patients, aged between 18 to 60 years, undergoing elective cardiac surgery in the department of cardiac anaesthesiology, G B Pant Institute of Postgraduate Medical Education and Research, New Delhi. Patients > 60 yrs of age and any known bleeding disorders were excluded from the study.

Outcome variables
Primary
Mortality in adult anaemic patients who underwent elective cardiac surgery and received blood transfusion

Secondary
Morbidity in adult anaemic patients who underwent elective cardiac surgery and received blood transfusion

METHODOLOGY:
All the preoperative parameters like the co-morbidities, the routine blood investigations, electrocardiograph, chest X-ray, echocardiography and angiography reports were documented. Written and informed consent was taken from the patients for surgery, anaesthesia and inclusion in the study. As per the departmental protocol, preoperative haemoglobin of 10 g/dl or greater was considered essential for fitness for elective cardiac surgery.

The patients were premedicated with intramuscular morphine (0.2 mg/kg) and promethazine 25 mg 1-2 hrs before surgery as per the institutional protocol. The baseline vital parameters, haemoglobin level, coagulation profile, other relevant investigations and risk assessment by Euroscore II were noted down.

Clinical monitoring included electrocardiography, invasive arterial pressure, central venous pressure, pulmonary artery pressure and pulmonary capillary wedge pressure (whenever necessary), and capnography. Patients were placed in supine position after placement of leads for electrocardiography. A wide bore peripheral venous cannula and access for invasive arterial line were obtained under local anaesthesia. General anaesthesia was induced as per institutional protocol using modest doses of fentanyl or morphine with thiopentone and midazolam. Choice of muscle relaxants (pancuronium, vecuronium or rocuronium) was at the discretion of the respective anaesthesiologist. Central venous access was obtained after endotracheal intubation with a triple lumen catheter or a sheath. A pulmonary artery catheter was floated through the sheath whenever necessary.

Standard CPB techniques using a membrane oxygenator were used for patients operated on CPB with a flow rate of 2.4 l/min/m2. Cold cardioplegia solution of 20 ml/kg was used for myocardial protection and repeated at a dose of 10 ml/kg every 30-45 minutes. Coronary stabilizer along with apical positioner was used for patients undergoing off-pump coronary artery bypass grafting (OPCAB). Unfractionated heparin was administered at an initial dose of 300 units/kg for surgery on CPB and at a dose of 150 units/kg for OPCAB. Subsequently, half of the initial dose was repeated after one hour. For the subsequent hours, quarter of the initial dose was repeated. Activated clotting time (ACT) of 400 seconds and 300 seconds were considered adequate for surgeries on CPB and OPCABs respectively. After completion of CPB or after the proximal anastomosis in OPCABs, protamine was administered at a dose of 1-1.3 mg/100 units of initial dose of heparin.

After adequate haemostasis and closure of the sternum, subcutaneous tissue and skin, patients were transferred to the intensive care unit (ICU) with endotracheal tube in situ for elective ventilation. The intraoperative parameters such as CPB time, aortic cross clamp time and transfusion requirements were noted. The vitals and arterial blood gas values were recorded immediately after transferring the patients to the ICU. Duration of ventilation (in hours), ICU stay (in days), hospital stay (in days), any surgical re-exploration, signs of infection [Fever (temperature >370C), Leucocytosis (White blood cell count >11000/mm3) or New opacities in chest X-ray] and perioperative kidney injury (≥ 50% increase in serum creatinine or decrease in urine output to < 0.5 ml/hr for > 6 hrs) were noted down. Bleeding (24 hour chest tube drainage), transfusion requirement and any other postoperative complications were also recorded.

Packed RBC (1 unit = 350 ml), FFP (1 unit = 120 ml), platelet concentrate (1 unit = 60 ml) and cryoprecipitate (1 unit = 60 ml) were used for transfusion. Transfusion was considered to have taken place, if any of the above products were transfused during the perioperative period. The decision to transfuse the blood and blood products was at the discretion of the respective surgical and anaesthesia team.

Sample size estimation
In order to detect 2.5% difference (Hung et. al, 2011) in mortality (in hospital death rate) between anaemic and non-anaemic cardiac surgery patients with 80% power and 95% confidence level and 1:1 ratio of anaemic and non-anaemic, a sample size of 1104 was required. Accordingly, the target number of 1100 patients was selected consecutively.

Statistical analysis:
Data were entered in MS Excel and analyzed using SPSS-26. In exploratory analyses, mortality and morbidity outcomes of elective cardiac surgery patients with and without anaemia, with and without transfusion were compared. Significance of association between qualitative parameters was assessed using Kruskal-Wallis test and Mann Whitney test. A p value <0.05 was considered as significant.

RESULTS:
A total number of 1538 continuous adult patients undergoing cardiac surgery were considered out of which 438 patients didn't meet the inclusion criteria [age < 18 yrs (n = 231), age >60 yrs (n = 157), emergency surgery (n = 41) and missing data (n = 9)] The patients were divided into 4 groups based on the presence of two criteria, i.e. anaemia and perioperative transfusion. The four groups were group AT (anaemic and transfused), group NT (non anaemic and transfused), group AN (anaemic and not transfused) and group NN (non anaemic and not transfused). Out of 1100 patients, Group AT, NT, AN and NN had 352, 481, 60 and 207 patients respectively.

Sex
Out of the 1100 patients included in the study, 696 (63.3%) were males whereas 404 (36.7%) patients were females. The group wise sex distribution was, group AT had 153 male patients and 199 female patients, group NT had 260 male and 221 female patients, group AN had 46 male and 16 female patients, while Group NN had 147 male and 60 female patients.(Table1)

Age
The mean age of patients in the study was 38.7 ± 12.7 yr. The mean age of patients in different groups was; group AT (38.2 ± 13.3 yr), group NT (38.4 ± 12.0 yr), group AN (38.3 ± 14.4 yr), group NN (40.0 ± 12.5 yr) (P = 0.370,Table 1).

Weight
The mean weight of patients in the study was 56.3 ± 11.5 kg. The mean weight of patients in different groups was; group AT (55.7 ± 10.9 kg), group NT (56.5 ± 12.2 kg), group AN (57.1 ± 12.1 kg), group NN (56.6 ± 10.5 kg) (P = 0.705,Table 1).

Height
The mean height of patients in the study was 158.8 ± 9.0 cm. The mean height of patients in different groups was; group AT (158.2 ± 8.0 cm), group NT (158.7 ± 9.5 cm), group AN (159.6 ± 10.5 cm), group NN (159.8 ± 8.7 cm) (P = 0.204, Table 1).

Haemoglobin
The mean haemoglobin concentration of the patients in the study was 13.3 ± 1.9 g/dl. Out of all the patients, 412 (37.5%) patients were anaemic with a mean haemoglobin level of 11.5 ± 1.1 g/dl whereas 688 (62.5%) patients were non anaemic with a mean haemoglobin level of 14.4 ± 1.4 g/dl (Table 1).

Co-morbidities
Out of the 1100 patients, 127 (11.5%) patients were diabetic, whereas 72 (6.5%) were hypertensive. Fourteen (1.3%) patients had thyroid disorder, 96 (8.7%) patients had chronic obstructive airway disorder, 55 patients (5.0%) gave history of tuberculosis, 40 patients (3.6%) had myocardial infarction and 14 patients (1.3%) had preoperative history of stroke (Table 1).

Type of surgery
There were a total number of 439 (39.9%) mitral valve replacements and 93 (8.5%) number of aortic valve replacements performed. Similarly, a total number of 254 (23.1%) OPCABs and 160 (14.5%) number of atrial septal defect repairs were performed. In addition, there were a total of 107 (9.7%) combined surgeries, whereas other surgeries (aortic surgeries, pericardiectomy, myxoma removal, ventricular septal defect repair etc.) were 47 (4.3%) in number (Table 1).

Number of transfusions:There were a total number of 6253 transfusions with a mean of 5.7 ± 6.1 transfusions per patient. The patients who did not receive any transfusion were 267 (24.3%) in number. Among the 833 (75.7%) patients who received transfusion, maximum (260, 23.6%) received a total of 3 transfusions.(Table1)

Mortality
There were a total number of 50 (4.5%) deaths during the study. Maximum number of deaths occurred in the group AT (35 deaths, 9.9%) where the patients were anaemic and received perioperative transfusion. The other groups where either one or none of the factors (i.e. anaemia and transfusion) were present had lesser number of deaths [group NT (12 deaths, 1.1%), group AN (1 death, 0.1%), group NN (2 deaths, 0.2%)].

The differences in mortality observed in the 4 groups were statistically significant (p < 0.001). When group AT was compared with the other three groups NT, AN and NN individually, there was statistically significant difference (p < 0.001, = 0.011, < 0.001 respectively). The non-anaemic patients who received transfusion also showed significantly higher mortality than those who did not receive transfusion (p = 0.022). When group AN was compared with group NT and group NN, no significant differences were found between the groups (p = 0.216 and p = 1.000 respectively) (Tables 2 and 4).

Morbidity
Morbidity in the study was measured by 5 parameters which were presence or absence of signs of infection [Fever (temperature >37^0C), Leucocytosis (White blood cell count >11000/mm^3) or New opacities in chest X-ray], presence or absence of perioperative renal injury (≥ 50% increase in serum creatinine or decrease in urine output to < 0.5 ml/hr for > 6 hrs), duration of ventilation (in hours), duration of ICU stay (in days) and duration of hospital stay (in days).

Infection
A total number of 325 (29.5%) patients showed signs of infection postoperatively during the study. Maximum number of patients had signs of infection in the Group AT (167, 15.2%) where the patients were anaemic and received perioperative transfusion. The other groups where either one or none of the factors (i.e. anaemia and transfusion) were present had lesser number of patients with infection [Group NT (131, 11.9%), Group AN (6, 0.5%), Group NN (21, 1.9%)].

The comparison of the groups on the basis of presence of infection was statistically significant ($p < 0.001$). When group AT was compared with the other three groups individually, there was a statistically significant difference ($p < 0.001$ in all three occasions). Similarly, when group NT was compared with group AN and NN, there was significant difference in the rate of infection ($p = 0.002$ and $p < 0.001$ respectively). But group AN and group NN did not show any difference ($p = 0.974$) (Tables 2 and 4).

Renal Injury
There were a total number of 257 (23.3%) patients who had postoperative renal injury during the study. Maximum number of patients in the group AT (130, 11.8%) had renal injury where the patients were anaemic and received perioperative transfusion. The other groups where either one or none of the factors (i.e. anaemia and transfusion) were present had lesser number of deaths [group NT (97, 8.8%), group AN (9, 0.8%), group NN (29, 2.6%)].

When compared on the basis of renal injury, all the 4 groups were statistically different from each other ($P < 0.001$). When group AT was compared with the other three groups individually, there was a statistically significant difference ($p < 0.001$ (AT vs NT), $p = 0.001$ (AT vs AN), $p < 0.001$ (AT vs NN)]. But when other groups were compared with each other, there was no significant difference [$p = 0.342$ (NT vs AN), $p = 0.056$ (NT vs NN), $p = 0.847$ (AN vs NN)] (Tables 2 and 4).

Duration of Ventilation
The mean duration of postoperative ventilation in all patients was 16.6 ± 29.9 hrs. Patients in group AT (27.6 ± 41.8 hrs) were ventilated for a longer duration than the groups NT (13.9 ± 25.0 hrs), AN (6.9 ± 2.1 hrs) and NN (6.9 ± 2.1 hrs).

When compared on the basis of duration of postoperative ventilation, all the 4 groups were statistically different from each other ($p < 0.001$). When group AT was compared with the other three groups individually, there was statistically significant difference ($p < 0.001$ in all the three comparisons). Patients in group NT had significantly increased duration of postoperative ventilation when compared with group NN ($p = 0.021$). But when group AN was compared with groups NT and NN, there was no significant difference ($p = 0.295$ and $p = 1.000$ respectively) (Tables 3 and 4).

Duration of ICU Stay
The mean duration of postoperative ICU stay in all patients was 5.0 ± 2.6 days. Patients in group AT (6.2 ± 3.2 days) stayed in the ICU for a longer duration postoperatively than the groups NT (4.7 ± 2.4 days), AN (3.9 ± 1.0 days) and NN (3.7 ± 1.0 days).

When compared on the basis of duration of postoperative ICU stay, all the 4 groups were statistically different from each other ($p < 0.001$). When group AT was compared with the other three groups individually, there was statistically significant difference ($p < 0.001$ in all the three comparisons). Patients in group NT had a significantly increased duration of postoperative ICU stay when compared with group NN ($p < 0.001$). But, when group AN was compared with groups NT and NN, there was no significant difference ($p = 0.090$ and $p = 0.950$ respectively) (Table 3 and 4).

Duration of Hospital Stay
The mean duration of postoperative hospital stay in all patients was 9.4 ± 3.8 days. Patients in group AT (11.6 ± 4.7 days) stayed in the hospital for a longer duration postoperatively than the groups NT (8.9 ± 3.5 days), AN (7.8 ± 1.4 days) and NN (7.5 ± 1.5 days).

When compared on the basis of duration of postoperative hospital stay, all the 4 groups were statistically different from each other ($p < 0.001$). When group AT was compared with the other three groups individually, there was statistically significant difference ($p < 0.001$ in all the three comparisons). Similarly, patients in group NT had significantly increased

duration of postoperative hospital stay when compared with group NN ($p < 0.001$). But, when group AN was compared with groups NT and NN, there was no significant difference ($p = 0.124$ and $p = 0.904$ respectively) (Tables 3 and 4).

Table 1: Distribution of patients in different groups along with the baseline characteristics.

Baseline Characteristics	Anaemic and transfused (Group AT)	Non anaemic and transfused (Group NT)	Anaemic and not transfused (Group AN)	Non anaemic and not transfused (Group NN)	P value
Total (N = 1100)	**N1 = 352**	**N2 = 481**	**N3 = 60**	**N4 = 207**	
Sex					
Male	153	260	46	147	
Female	199	221	16	60	
Age (In years)	38.2 ± 13.3	38.4 ± 12.0	38.3 ± 14.4	40.0 ± 12.5	0.370(NS)
Weight (In Kg)	55.7 ± 10.9	56.5 ± 12.2	57.1 ± 12.1	56.6 ± 10.5	0.705(NS)
Height (In cm)	158.2 ± 8.0	158.7 ± 9.5	159.6 ± 10.5	159.8 ± 8.7	0.204(NS)
Preoperative Hb	11.3 ± 1.1	14.2 ± 1.4	12.4 ± 0.6	14.9 ± 1.3	
Co-morbidities					
Diabetes	43	51	8	25	
Hypertension	21	33	4	14	
Tuberculosis	18	23	3	11	
Hypothyroidism	4	6	1	3	
History of MI	15	18	2	5	
Stroke	5	7	0	2	
COAD	31	38	8	19	
Surgeries					
MVR	158	205	18	58	
AVR	33	42	4	14	
OPCAB	69	92	22	71	
ASD Repair	34	67	12	47	
Combined Surgery	41	55	2	9	
Others	17	20	2	8	

Table 2: Comparison mortality, infection and renal injury among different four groups.

Qualitative Parameters	Anaemic and transfused (Group AT)	Non anaemic and transfused (Group NT)	Anaemic and not transfused (Group AN)	Non anaemic and not transfused (Group NN)	P - value
Death	35	12	1	2	< 0.001(HS)
Infection	167	131	6	21	< 0.001(HS)
Renal Injury	130	97	9	29	< 0.001(HS)

Table 3: Comparison duration of ventilation, ICU stay and hospital stay among four groups.

Quantitative Parameters	Anaemic and transfused (Group AT)	Non anaemic and transfused (Group NT)	Anaemic and not transfused (Group AN)	Non anaemic and not transfused (Group NN)	P - value
Duration of ventilation (In hours)	27.6 ± 41.8	13.9 ± 25.0	6.9 ± 2.1	6.9 ± 2.1	< 0.001(HS)
Duration of ICU stay (In days)	6.2 ± 3.2	4.7 ± 2.4	3.9 ± 1.0	3.7 ± 1.0	< 0.001(HS)
Duration of hospital stay (In days)	11.6 ± 4.7	8.9 ± 3.5	7.8 ± 1.4	7.5 ± 1.5	< 0.001(HS)

Table 4 showing comparison of various groups as isolated pairs on the basis of various parameters of morbidity and mortality (AT: anaemic and transfused, NT: non anaemic and transfused, AN: anaemic and not transfused, NN: non anaemic and not transfused)

Parameters	AT vs NT	AT vs AN	AT vs NN	NT vs AN	NT vs NN	AN vs NN

Duration of ventilation (In hours)	< 0.001	< 0.001	< 0.001	= 0.295	= 0.021	= 1.000
Duration of ICU stay (In days)	< 0.001	< 0.001	< 0.001	= 0.090	< 0.001	= 0.950
Duration of hospital stay (In days)	< 0.001	< 0.001	< 0.001	= 0.124	< 0.001	= 0.904
Death	< 0.001	= 0.011	< 0.001	= 0.216	= 0.022	= 1.000
Infection	< 0.001	< 0.001	< 0.001	= 0.002	< 0.001	= 0.974
Renal injury	< 0.001	= 0.001	< 0.001	= 0.342	= 0.056	= 0.847

DISCUSSION:

In this study, it was found that 37.5% adult patients undergoing elective cardiac surgery had preoperative anaemia. It was observed that those who were anaemic and received transfusion suffered from higher mortality and morbidity (postoperative infection, renal injury, duration of ventilation, ICU and hospital length of stay) as compared to those who were not anaemic and/or not transfused.

Prevalence of anaemia

The prevalence of anaemia in India at community level is significantly higher as compared to the world standards. Likewise, the prevalence of anaemia in patients undergoing cardiac surgery is also high. In the present study comprising of 1100 adult patients undergoing elective cardiac surgery, 412 were found to be anaemic. So, the prevalence of anaemia was 37.5% which is lower than the community standards in India. This might be due to the institutional protocol of optimization of haemoglobin level to 10 g/dl before accepting the patients for elective cardiac surgery. Also, the exclusion of emergency surgeries might have played a role.

Joshi et al found a similar prevalence of anaemia (37.1%) in patients undergoing valvular heart surgeries.[45] As majority of patients (58.1%) in our study underwent valvular surgeries, so the similarity in patient profile might have been the reason behind this similarity.

The distribution of anaemic patients as per sex (33.91% among males and 40.88% among females) showed more prevalence of anaemia in female patients than their male counterparts by Joshi et al.[17] This effect was even more pronounced in our study (28.59% among males and 53.21% among females) as majority of females belonged to the reproductive age group (mean age 35.5 ±11.4 years).

In the study by Borde et al**Error! Bookmark not defined.**, the prevalence of anaemia was found to be higher i.e. 51.95% in patients with rheumatic heart disease undergoing cardiac surgery. The prevalence of mild anaemia [male (11.0 – 12.9 g/dl) and female (11.0 – 11.9 g/dl)] was 33.15% whereas that of moderate anaemia (8.0 – 10.9 g/dl for both sexes) was 18.80%. As in our study, only patients with more than 10 g/dl were accepted for elective cardiac surgery due to institutional protocol, the prevalence was expected to be higher than the patients with mild anaemia, but lower than the overall prevalence as many of the patients with moderate anaemia were optimized prior to surgery.

Transfusion requirement:

Patients undergoing cardiac surgery are likely to require more transfusion due to the nature of surgery (on vascular structures), CPB effects such as haemodilution and inflammatory response, and coagulation abnormalities among others. Indeed, cardiac surgery is considered as the largest consumer of blood and blood products and the number of patients requiring transfusion is as high as 80 percent. In the present study, a total number of 833 patients (75.7%) were given blood or blood products transfusion. There have been efforts to optimise the blood transfusion during cardiac surgery and restrictive and liberal transfusion policies have emerged.

In a multi-centric trial consisting of 5243 adult patients undergoing cardiac surgery by Mazer et al[18], PRBC transfusion occurred in 52.3% of the patients in the restrictive-threshold group, as compared with 72.6% of those in the liberal-threshold group. A large percentage of patients requiring transfusion in the present study may be related to the smaller size of the patients (mean weight 56.3 ± 11.5 kg), as one of the important factors determining the transfusion requirement is the blood volume of the patients. In addition, the decision to transfuse was left to the discretion of the respective anaesthesia and surgical team, some of which may have resorted to liberal transfusion.

Mortality

The overall mortality in our study was found to be 4.5% (50 out of 1100 patients). When comparison was made between the anaemic (36 deaths, 8.7%) and non-anaemic (14 deaths, 2.0%) patients, there was significantly increased percentage of deaths in the anaemic group ($p < 0.001$). Similarly, increased mortality was also observed in the patients who received transfusion (47 deaths, 5.6%) than those who did not receive transfusion (3 deaths, 1.1%) perioperatively. Mortality rate

was highest when anaemic patients were given transfusion (Group AT – 35 deaths, 9.9%) than the other three groups. The presence of significantly higher mortality in anaemic patients who received transfusion (9.9%) confirms the additive effect of both anaemia (8.7%) and transfusion (5.6%) when present together.

In a large multi-centric trial TITRe2 by Reeves et al[19], the mortality was found to be 4.2% which is similar to our study. There were 17 (2.7%) cases of mortality in the 622 patients (31%) who didn't receive PRBC transfusion. The higher death rate in patients not transfused with PRBC might be explained by the role of blood products other than PRBC (21.2%, 28.3% and 6.9% received FFP, platelet and cryoprecipitate transfusion respectively).

In a study by Vlot et al[20], intraoperative RBC transfusion was associated with a more than three-fold mortality risk (OR 3.1; 95% CI 1.5–6.7; P = 0.003). In patients with the highest probability of transfusion, intraoperative RBC transfusion was associated with a 4.1-fold risk of mortality (PS adjusted OR 4.1 and 95% CI 1.3–12.6, P = 0.016). The OR for RBC associated mortality changed with 7% after adding plasma transfusion (OR 3.8, P = 0.021).

Morbidity

Five predetermined parameters (rate of postoperative infection, renal injury and duration of ventilaton, ICU stay and hospital stay) were used in the study to find out morbidity in the patients.

Infection

A total number of 325 patients (29.5%) showed signs of postoperative infection in the study as per the predetermined criteria. When comparison was made between the anaemic (173, 42.0%) and non anaemic (153, 22.2%) patients, there was significantly increased percentage of patients showing infection in the anaemic group. Similarly, increased rate of infection was also found in the patients who received transfusion (298, 35.8%) than those who didn't receive transfusion (27, 10.1%) perioperatively. So, both anaemia and transfusion did increase the rate of postoperative infection independently in patients undergoing cardiac surgery.

Infection rate was highest in Group AT where anaemic patients were given transfusion (167, 47.4%) than the other three groups. The presence of significantly higher rate of infection in anaemic patients who received transfusion confirms the additive effect of both anaemia and transfusion when present together.

In the meta-analysis by Padmanabhan et al[21], seven studies (23,863 patients) reported on infection after cardiac surgery. Anaemic patients were found to be at higher risk of developing postoperative infection compared with non anaemic patients (OR, 2.65; 95% CI, 1.98-3.55; P < .001). Our study also found similar results (OR, 2.42; 95% CI, 1.86-3.16; P < .001) concluding anaemic patients undergoing cardiac surgery to be at 2.4 times higher risk of developing infection than non anaemic patients.

The study also found a 5.1 times higher chances in patients who received transfusion than those who didn't receive transfusion (OR, 5.11; 95% CI, 3.35-7.79; P < .001).

Renal Injury

A total number of 257 patients (23.3%) showed signs of postoperative renal injury in the study as per the predetermined criteria. When comparison was made between the anaemic (139, 33.7%) and non anaemic (126, 18.3%) patients, there was significantly increased percentage of patients showing renal injury in the anaemic group. Similarly, increased rate of renal injury was also found in the patients who received transfusion (227, 27.3%) than those who didn't receive transfusion (38, 14.2%) perioperatively. So, both anaemia and transfusion did increase the rate of postoperative renal injury independently in patients undergoing cardiac surgery.

Postoperative renal injury was highest in Group AT where anaemic patients were given transfusion (130, 37.0%) than the other three groups. The presence of significantly higher rate of renal injury in anaemic patients who received transfusion confirms the additive effect of both anaemia and transfusion when present together.

In a study by Lapar et al, PRBC transfusion was associated with a 6 fold stronger association with renal failure (OR 6.3, P < 0.001) whereas anaemia when compared with a haematocrit of 40% was associated with a 3 times more chance of renal failure.[22]

Our study also found similar results (OR, 2.27; 95% CI, 1.71-3.01; P < .001) concluding anaemic patients undergoing cardiac surgery to be at 2.3 times higher risk of developing infection than non anaemic patients. (Figure 17) The study also found a 2.3 times higher chances in patients who received transfusion than those who didn't receive transfusion (OR, 2.25; 95% CI, 1.55-3.29; P < .001).

Duration of ventilation

The mean duration of ventilation was 16.6 ± 29.9 hrs in the study population. When comparison was made between the anaemic (24.6 ± 39.3 hrs) and non anaemic (11.8 ± 21.1 hrs) patients, there was significantly increased duration of postoperative ventilation in the anaemic group ($P < 0.001$). Similarly, increased duration of ventilation was also found in the patients who received transfusion (19.6 ± 33.8 hrs) than those who didn't receive transfusion (6.9 ± 2.1 hrs) perioperatively ($P < 0.001$). So, both anaemia and transfusion did increase the duration of postoperative ventilation independently in patients undergoing cardiac surgery.

The duration of postoperative ventilation was highest in Group AT where anaemic patients were given transfusion (27.6 ± 41.8 hrs) than the other three groups ($P < 0.001$). The presence of significantly higher duration of ventilation in anaemic patients who received transfusion confirms the additive effect of both anaemia and transfusion when present together.

In a study by Kim et al, anaemia was significantly associated with prolonged ventilation time (47.01 hours vs. 23.59 hours, $P = 0.0076$) when compared to non anaemic patients.[23]

Duration of ICU stay

The mean duration of ICU stay was 5.0 ± 2.6 days in the study population. When comparison was made between the anaemic (5.9 ± 3.1 days) and non anaemic (4.4 ± 2.2 days) patients, there was significantly increased duration of postoperative ICU stay in the anaemic group ($P < 0.001$). Similarly, increased duration of ICU stay was also found in the patients who received transfusion (5.3 ± 2.9 days) than those who didn't receive transfusion (3.8 ± 1.1 days) perioperatively ($P < 0.001$). So, both anaemia and transfusion did increase the duration of postoperative ICU stay independently in patients undergoing cardiac surgery.

The duration of postoperative ICU stay was highest in Group AT where anaemic patients were given transfusion (6.2 ± 3.2 days) than the other three groups ($P < 0.001$). The presence of significantly higher duration of ICU stay in anaemic patients who received transfusion confirms the additive effect of both anaemia and transfusion when present together.

De Santo et al. reported that anaemic patients remained in the ICU on average 1 day longer than non-anaemic patients (3.9 vs 2.9 days, $P < 0.001$).[24]

Duration of hospital stay

The mean duration of hospital stay was 9.4 ± 3.8 days in the study population. When comparison was made between the anaemic (11.0 ± 4.5 days) and non anaemic (8.4 ± 2.9 days) patients, there was significantly increased duration of hospital stay in the anaemic group ($P < 0.001$). Similarly, increased duration of hospital stay was also found in the patients who received transfusion (10.0 ± 4.1 days) than those who didn't receive transfusion (7.8 ± 1.5 days) perioperatively ($P < 0.001$). So, both anaemia and transfusion did increase the duration of hospital stay independently in patients undergoing cardiac surgery.

The duration of hospital stay was highest in Group AT where anaemic patients were given transfusion (11.6 ± 4.7 days) than the other three groups ($P < 0.001$). The presence of significantly higher duration of hospital stay in anaemic patients who received transfusion confirms the additive effect of both anaemia and transfusion when present together. In a study by Loor et al, patients with any negative exposure to anemia and RBC transfusion had longer postoperative hospital stay than patients without negative exposures.[25]

CONCLUSION:

Prevalence of anaemia is high in adult Indian patients undergoing elective cardiac surgery. Community level interventions like better dietary habits, iron supplements or treatment of worm infestations are needed to decrease the prevalence of anaemia. Anaemia and perioperative transfusion independently increase morbidity and mortality in adult patients undergoing elective cardiac surgery. But when both factors are present together, there is significant increase in mortality and morbidity than any one factor alone. All the parameters of morbidity were significantly higher in anaemic patients who received transfusion. So we advise preoperative optimisation of anaemia in elective cardiac surgeries along with avoidance of unnecessary blood products transfusion perioperatively.

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