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EVALUATING THE IMPACT OF FRESH FROZEN PLASMA (FFP) VERSUS NON-FFP PRIMING ON POSTOPERATIVE BLEEDING IN CHILDREN <10 YEARS UNDERGOING CARDIAC SURGERY: A PROSPECTIVE SINGLE-CENTER EXPERIENCE BELAGAVI, KARNATAKA.

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ABSTRACT :

Background

Limited research in India has explored the use of fresh frozen plasma (FFP) as a priming solution in pediatric open-heart surgery. The optimal cardiopulmonary bypass (CPB) circuit priming solution remains debated

Objective

This study aimed to evaluate the effects of FFP versus non-FFP priming solutions on metabolic variables, coagulation profiles, postoperative bleeding, and colloidal oncotic pressure in pediatric Cardiopulmonary bypass patients at the tertiary care hospital of Belagavi, Karnataka

Methods

A prospective observational study was conducted at a tertiary care hospital in Karnataka. Sixty-four pediatric patients under 10 years undergoing elective open heart surgery requiring CPB were randomly assigned to receive either FFP (FFP group) or non-FFP (Non-FFP group) as a priming solution. Preoperative clinical, biochemical, and demographic data were collected. Postoperative outcomes were assessed in terms of chest drain bleeding, coagulation profile, blood product requirements, and morbidity within 24 hours.

Results

No significant difference in chest drain bleeding was observed between the groups. The FFP group showed higher mean arterial pressure during CPB cooling and rewarming. The Non-FFP group required more blood transfusions, while the FFP group maintained a better coagulation profile.

Keywords:Prospective study, Fresh frozen plasma, Bleeding, Colloidal oncotic pressure

Introduction

The cardiopulmonary bypass (CPB) approach utilizes a heart-lung device to briefly take over the heart and lungs during a cardiac procedure.[1] This provides a bloodless surgical field while simultaneously maintaining oxygenation and circulation.[1] The components of CPB include a roller pump head,

a hardshell venous reservoir, a membrane oxygenator, arterial and venous cannulas, an arterial filter, and tubing made of polyvinyl chloride (PVC) and silicone.[1] During CPB, deoxygenated blood is drained by gravity into the venous reservoir, and the blood is actively pumped forward through the roller pump to the oxygenator, where oxygenation and heat exchange occur before the blood is returned to the arterial cannula and subsequently into the systemic circulation.[1] CPB circuits must be primed with crystalloid and colloid solutions to ensure adequate volume levels and maintain maximum CPB flow rates without the risk of microemboli.[2,3] Crystalloids are commonly used as a transparent priming solution. They cause hemodilution; however, they fail to maintain circulating oncotic pressure.[3,4] In contrast, colloids are plasma expanders that help maintain higher colloidal oncotic pressure and reduce tissue edema.[3,4]

In pediatric open-heart surgery, priming solutions aim to minimize the side effects caused by the dilution of red blood cells, coagulation factors, and other plasma proteins.[5] Blood component dilution occurs due to the use of large CPB circuits relative to the patient's body surface area.[6] Using fresh frozen plasma (FFP) as part of the prime solution helps reduce bleeding, the need for blood transfusions, and maintains hemoglobin and hematocrit levels.[7] Hemodilution, caused by these solutions, can increase fluid movement into the extracellular space, lower circulating colloidal oncotic pressure, cause coagulation abnormalities, lead to postoperative weight gain, dilute plasma proteins, and potentially result in organ dysfunction.[6,7] FFP is a component of blood that comprises antithrombin, immunoglobulins, albumin, and coagulation factors.[7,8] Coagulation factors and fibrinogen levels tend to decrease with prolonged CPB due to protein denaturation.[7] The ideal priming solution for CPB remains a topic of debate in open-heart surgery.[8] Pediatric patients undergoing surgery with CPB often require blood products postoperatively.[9,11] The use of priming solutions, which have a greater volume than the patient's predicted blood volume, causes hemodilution, significantly reducing coagulation factors and platelet count. In cyanotic pediatric patients, a hematocrit greater than 30% is desired during CPB, while a cyanotic patient should have a hematocrit of no less than 25%.[11] The question of whether to prime the CPB circuit with FFP or to administer FFP after weaning from CPB to reduce postoperative bleeding remains controversial in pediatric heart surgery.[11,12] Pediatric patients are at higher risk for thrombotic events during CPB due to their lower body weight and developmental differences in their hematological systems.[12] This can lead to a decrease in coagulation factors, a 50% reduction in antithrombin III levels, and a 70% reduction in platelet count, increasing the risk of postoperative bleeding[9,10] Colloidal oncotic pressure (COP) is a key indicator of hemodilution during CPB in cardiac surgery. COP during CPB should be maintained above 15 mmHg.[9,13] Low circulating oncotic pressure during CPB can cause edema in vital organs and extravascular tissue spaces.[13] COP plays an essential role in fluid management between the intravascular and extravascular spaces due to fluctuations in hydrostatic pressure between the interstitial space and the capillaries of the cell membrane.[9,13,14]

MATERIALS AND METHODS

Study Design:

Prospective Case-Control Study

Source of Data:

Paediatric subjects undergoing open-heart surgery requiring cardiopulmonary bypass (CPB) in the Department of Cardiovascular and Thoracic Surgery, KLE's Dr. Prabhakar Kore Hospital and Research Centre, Belgaum, Karnataka, India.

Study Period:

June 2024 – March 2025

Sample Size:

Sample size calculation:

Sample size (n_1) = $((z_1\text{-}\alpha/_2 + z_1\text{-}\beta)^2 (SD_1^2 + SD_2^2)) / (\bar{x_1} - \bar{x_2})^2$

$= (1.96 + 1.29)^2 (9 + 8) / (41 - 34)^2$

$= 1531.2 / 49$

$n_1 = 31.25 \approx 32$

Thus, $n_1 = 32$ per group.

Total sample size (n) = 32 × 2 = 64

Where:

$Z_{1-\alpha/2}$ (95%) = 1.96

$Z_{1-\beta}$ (90%) = 1.29

$\bar{x_1}$ = 41 (mean of the first group)

$\bar{x_2}$ = 34 (mean of the second group)

SD_1 = 9 (standard deviation of the first group)

SD_2 = 8 (standard deviation of the second group)

n_1 = sample size of one group

Inclusion Criteria:

Patients < 10 years of age undergoing cardiac surgery
Presence of congenital heart disease
Patients who opted for surgery
Attendants willing to participate in the study

Exclusion Criteria:

Patients > 10 years of age
Emergency surgery
Patients with coagulation-related diseases
Patients with sepsis
Patients on anticoagulation therapy
Attendants not willing to participate in the study

Data Collection Procedure:

Sixty-four subjects under the age of 10 who underwent cardiac surgery requiring cardiopulmonary bypass (CPB) at the Department of Cardiothoracic and Vascular Surgery (CTVS), KLE's Dr. Prabhakar Kore Hospital and Research Center, and fulfilled the inclusion criteria were involved in this study. The group that received fresh frozen plasma (FFP) was labeled the FFP group, while the group that did not receive FFP was labeled the non-FFP group. The demographic and preoperative clinical characteristics of all study participants were recorded. During the intraoperative period, operative and cardiopulmonary bypass variables were also noted. Preoperative coagulation profiles, including biochemical markers such as Prothrombin Time (PT), Activated Partial

Thromboplastin Time (aPTT), International Normalized Ratio (INR), and Activated Clotting Time (ACT), were recorded. Preoperative colloidal oncotic pressure (COP) was calculated using biochemical markers such as albumin, globulin, total protein, and the albumin-globulin ratio. Intraoperative COP was calculated using an electronic perfusion calculator. Baseline hemoglobin (Hb), hematocrit (Hct), serum lactate, and urine output were noted before the initiation of cardiopulmonary bypass.

During the conduct of cardiopulmonary bypass, circulating COP, CPB blood flows, ACT, Mean Arterial Pressure (MAP), and serum lactate were noted at the initiation, during the cooling phase, and the rewarming phase of CPB. After weaning from CPB, MAP, serum lactate, ACT, and patient nasal temperature were recorded.

The participants were followed up in the postoperative period to assess immediate postoperative outcomes. Data on study variables were obtained 24 hours after the surgery. Changes in hemoglobin, hematocrit, serum lactate, and coagulation profiles (such as PT, aPTT, INR) were observed and recorded. Urine output was also noted.

The total volume of bleeding and transfusion of blood components such as packed red blood cells, fresh frozen plasma, and platelet concentrate during the first 24 hours post-surgery was documented. Additionally, the patient's weight gain or weight loss was recorded 24 hours after the surgery.

Subjects were followed for postoperative outcome variables, including the total amount of blood component transfusion, bleeding, the requirement for mechanical cardiovascular support (such as Extracorporeal Membrane Oxygenation [ECMO]), arterial blood gas (ABG) analysis preoperatively, intraoperatively, and postoperatively. During the study, institutional protocols for blood transfusions, perioperative mean arterial blood pressure control, and maintenance of perioperative hemodynamic and perfusion pressure were strictly followed.

Formula for calculation of maximum CPB blood flow of CPB (De-bouse formula)

$$\underset{\text{(L/min)}}{\text{CPB Flow Rate}} = \underset{\text{(m}^2\text{)}}{\text{Body Surface Area}} \times \underset{\text{(L/min/m}^2\text{)}}{\text{Cardiac Index}}$$

Cardiac Index varies depending on age and temperature.

Formula for calculation of Colloid Oncotic Pressure (COP)

COP = (4.0814×A/G×TP)/(A/G+0.0153×TP) mmHg

Where,

A/G = Albumin Globulin Ratio

TP = Total Protein

Circulating colloidal oncotic pressure was calculated by using the online electronic perfusion Calculator.

Ethical Consideration: Ethical approval was obtained from the JNMC Institutional Ethical Committee. **Ref No: MDC/JNMCIEC/311 dated: 29/05/2024**

Data Analysis /Statistical Analysis:

Data from 64 pediatric subjects aged below 10 years undergoing cardiac surgery were collected and entered microsoft excel sheet. Data was analyzed using SPSS software version 29 and Microsoft Office Excel software version 2021.

Descriptive statistics were computed for the study variables. Mean and Standard Deviation (SD) were computed for continuous variables. Frequency and percentage were computed for categorical variables.

An independent t-test was used to compare the means between the FFP and Non- FFP groups. The level of significance was set at 5% ($p < 0.05$).

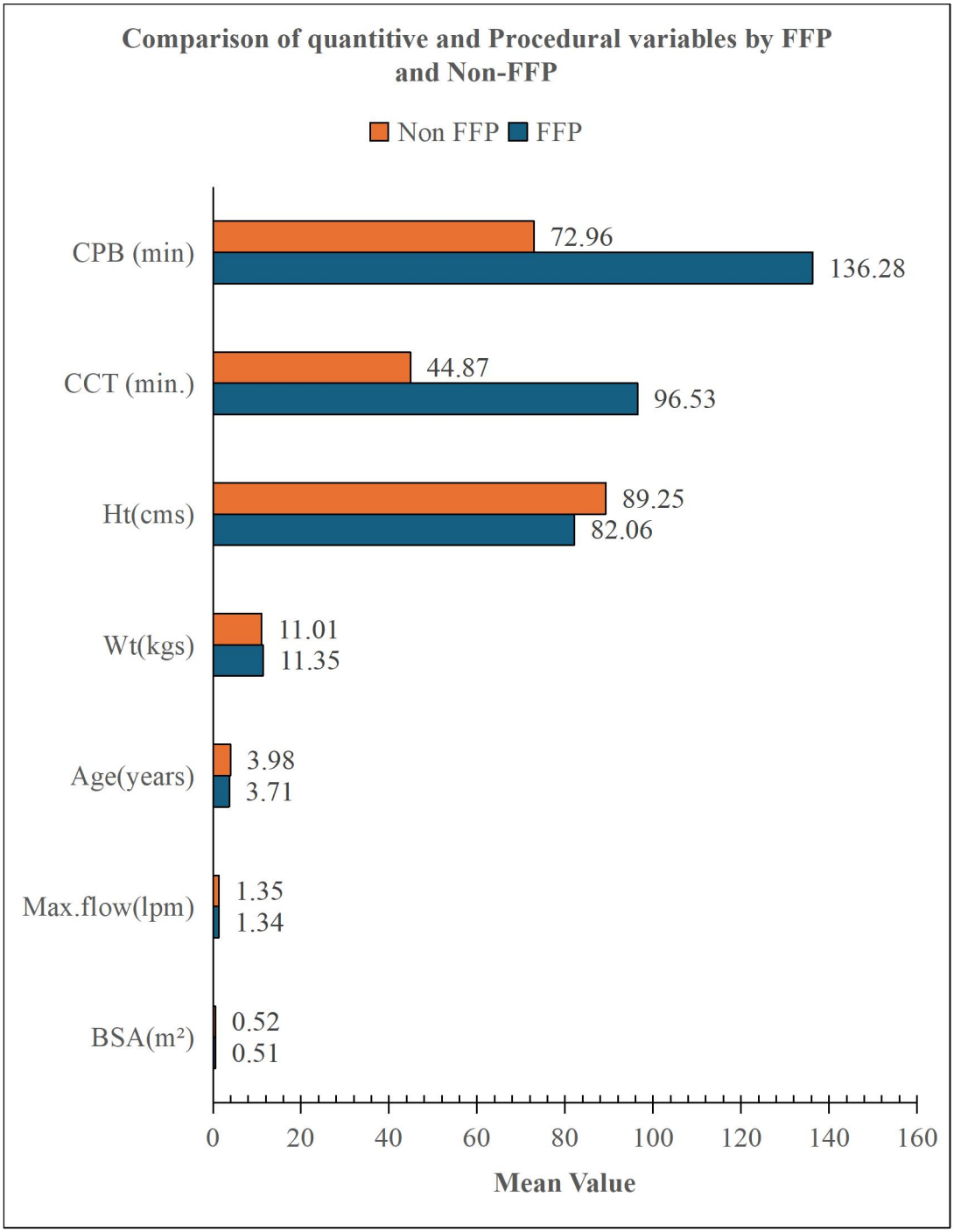
Results

Table 1. Comparison of Quantitative and Procedural Characteristics Between FFP and Non- FFP Group

Variable	FFP	Non FFP	t value	p value
	Mean ± SD	Mean ± SD		
Age(years)	3.71 ± 3.82	3.98 ± 2.79	-0.31	0.754
Height (cm)	82.06 ± 34.47	89.25 ± 22.66	-0.98	0.328
Weight(kg)	11.35 ± 7.46	11.01 ± 4.6	0.22	0.827
Body surface area (m^2)	0.51 ± 0.26	0.52 ± 0.17	-0.16	0.873
Max. flow(lpm)	1.34 ± 0.65	1.35 ± 0.42	-0.16	0.873
Cross clamp time(min.)	96.53 ± 58.04	44.87 ± 30.72	4.44	**<0.001**
Cardiopulmonary bypass time(min)	136.28 ± 75.98	72.96 ± 36.35	4.24	**<0.001**

Subjects available for the study were divided into two groups of priming cardiopulmonary bypass circuit, namely “FFP” and “Non-FFP” groups.

The mean age of the subjects in the “FFP” group was 3.71 ± 3.82 respectively 3.98 ± 2.79 years in the “non-FFP” group. The average body surface area (BSA) in the “FFP” group was 0.51 ± 0.26 and 0.52 ± 0.17 m^2 in the “non-FFP” group. The mean flow rate of cardiopulmonary bypass was 1.34 ± 0.65 l/min in the “FFP” group over 1.35 ± 0.42 l/min in the “non-FFP” group. These parameters were statically non-significant. The mean cross clamp time in the “FFP” group was 96.53 ± 58.04 and 44.87 ± 30.72 minutes in the “non-FFP” group, which was significantly higher in the “FFP” group. Most of the patients in the fresh frozen plasma were complex congenital heart disease, so, the correction of the defect took prolong time. The average time taken for the cardiopulmonary bypass time in the “FFP” group was 136.28 ± 75.98 over 72.96 ± 36.35 minutes in the “non-FFP” group, which was also statistically significantly higher in “FFP” group as seen in graph 1, table 1.



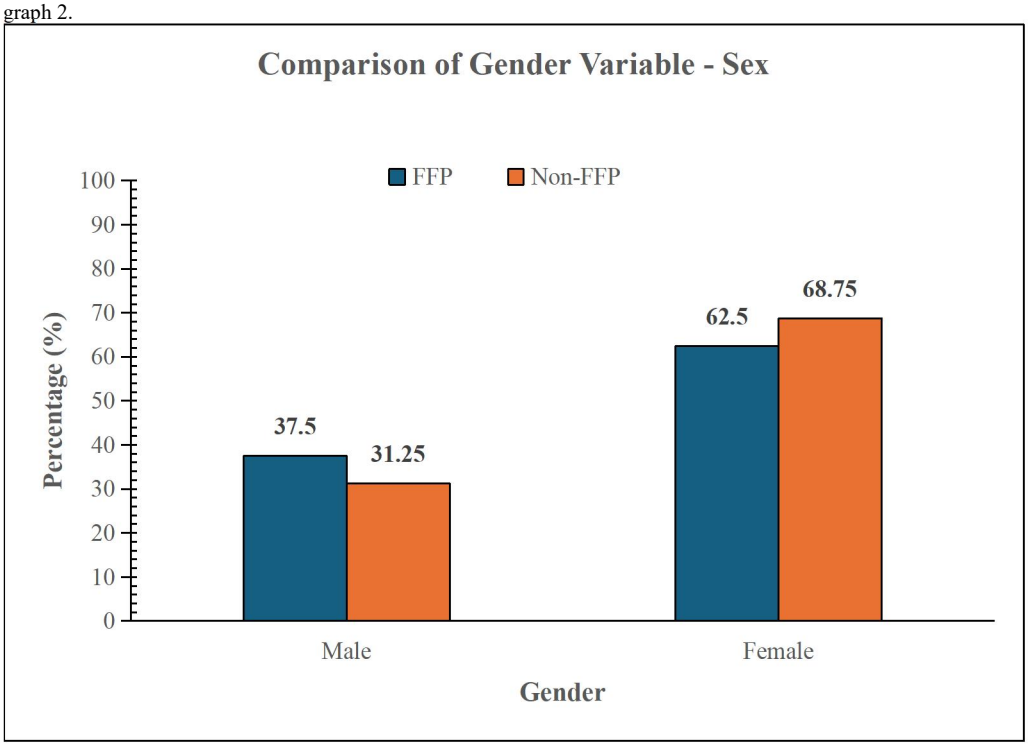
Graph 1. Comparison of Quantitive and Procedural Characteristics Between "FFP" and "Non FFP" Group

Table 2. Comparison of Gender Between "FFP" contrast to "Non-FFP" Group

	FFP		Non-FFP		Total (64)	
	n (32)	%	n (32)	%	n (64)	%
Male	12	37.5	10	31.25	22	34.37

Female	20	62.5	22	68.75	42	65.62

There were 12 males (37.5%) and 20 females (62.5%) in "FFP" group vs 10 males (31.25%) and 22 females (68.75%) in "Non FFP" group. There was total 22 (34.37%) and females 42 (65.62%) in both "FFP" and "Non FFP" group as seen in the table 2, graph 2.



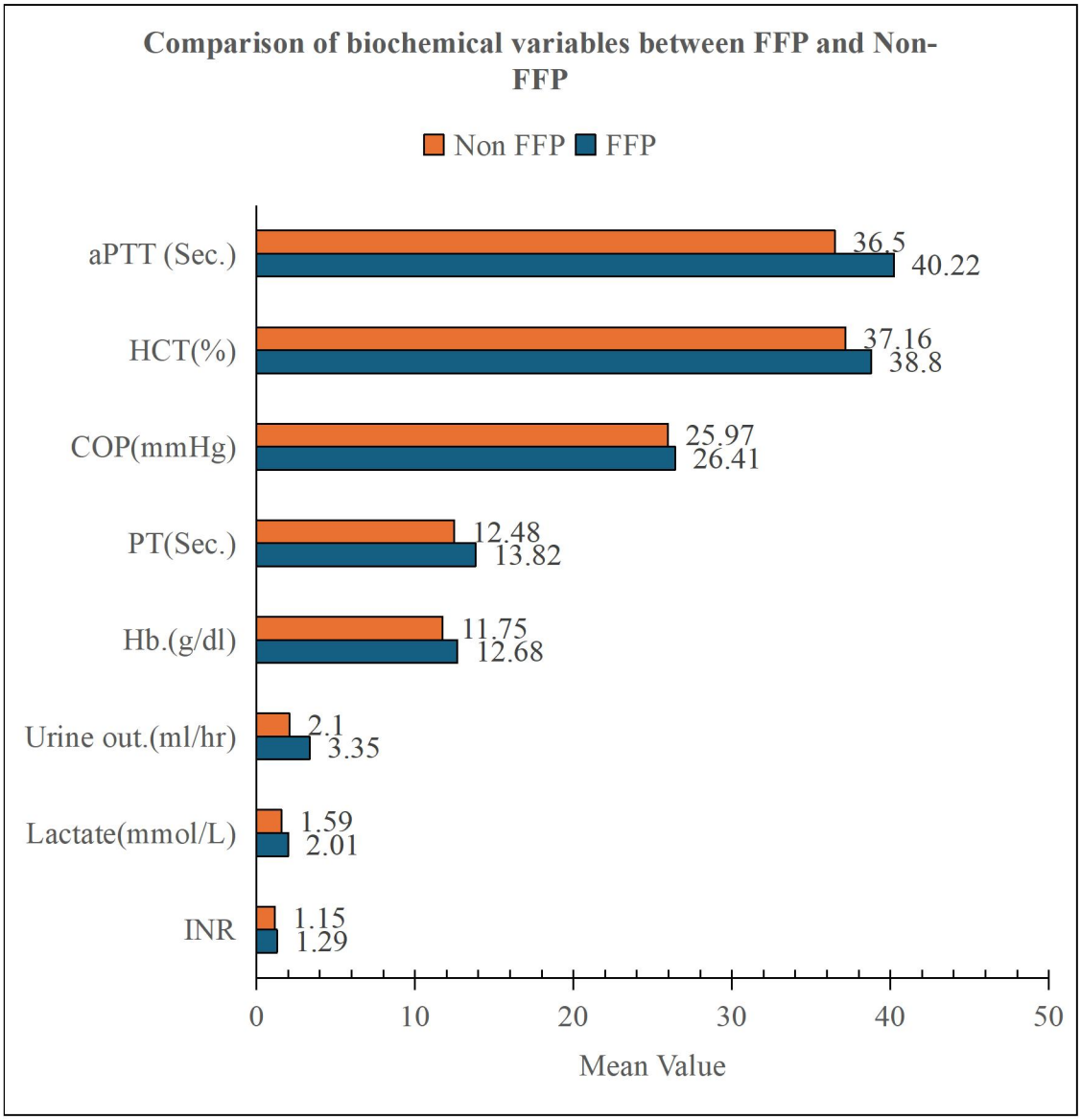
Graph 2. Comparison of Gender Between "FFP" contrast to "non-FFP" Group

Table 3. Comparison of biochemical Variables In "FFP" as opposed to "Non FFP" Group - Baseline

Variable	FFP	Non FFP	t value	p value
	Mean ± SD	Mean ± SD		
Hemoglobin (g/dl)	12.68 ± 2.50	11.75 ± 1.55	1.782	0.08
Hematocrit (%)	38.8 ± 7.07	37.16 ± 6.20	0.983	0.33
Platelet Count (Plt/µl)	344875 ± 107627.71	379062.5 ± 139695.96	-1.097	0.277
Serum Lactate(mmol/L)	2.01 ± 1.04	1.59 ± 0.64	1.897	0.063
Urine output (ml/hr)	3.35 ± 5.64	2.10 ± 2.072	1.184	0.241
Prothrombin time (S)	13.82 ± 1.79	12.48 ± 1.14	3.529	**<0.001**
Activated partial thromboplastin time(aPTT)(S)	40.22 ± 6.03	36.5 ± 3.75	2.961	**0.004**
Colloid oncotic pressure (mmHg)	26.41 ± 3.30	25.97 ± 2.22	0.637	0.527

International narmalized ratio (INR)	1.29 ± 0.22	1.15 ± 0.10	3.08	**0.003**

The mean hemoglobin in the "FFP" group was 12.68 ± 2.50 and 11.75 ± 1.55 g/dl in "non-FFP" group. The mean hematocrit (Hct) in "FFP" group was 38.8 ± 7.07 vs. 37.16 ± 6.20 % in "Non FFP" group. The mean platelet count in "FFP" group was 344875 ± 107627.71 and 379062.5 ± 139695.96 Plt/µl in "non-FFP" group. The mean lactate level in the "FFP" group was 2.01 ± 1.04 respectively 1.59 ± 0.64 mmol/l in the "non-FFP" group. The mean urine output in the "FFP" group was 3.35 ± 5.64 and 2.10 ± 2.072 ml/hr in the "non-FFP" group. This data was not statistically significant. The mean prothrombin time (PT) in the "FFP" group was 13.82 ± 1.79 vs. 12.48 ± 1.14 second in the "non-FFP" group, which was statically significant. However, it was not clinically significant as it was within the normal range. The mean activated partial thromboplastin time (aPTT) in the "FFP" group was 40.22 ± 6.03 and 36.5 ± 3.75 second in the "non-FFP" group, which was statistically significant. However, it was not clinically significant as it was within the normal range. The mean colloid oncotic pressure in the "FFP" group was 26.41 ± 3.30 vs. 25.97 ± 2.22 in the "non-FFP" group. The international normalized ratio in the "FFP" Group was 1.29 ± 0.22 vs. 1.15 ± 0.10 14 in "non-FFP" group which was statically significant. However, it was not clinically significant as it was within the normal range as seen in the table 3, graph 3.



Graph 3. Comparison biochemical Variables between "FFP" and "Non-FFP" Group - Baseline

Table 4 Comparison of Operative & Biochemical Variables In "FFP" and "Non-FFP" Group, During the Conduct of CPB

	Variable	FFP	Non FFP	t value	p value
		Mean ± SD	Mean ± SD		
Initiation	Flow (LPM)	1.14 ± 0.76	1.14 ± 0.76	1.439	0.155
	MAP	42.46 ± 9.12	45.53 ± 9.51	-1.314	0.194
	ACT (sec.)	750.12 ± 194.10	631.84±163.29	2.638	**0.011**
	Temp.	35.19 ± 0.88	35.65 ± 1.75	-1.313	0.194
	Lactate	2.43 ± 1.30	2.17 ± 0.94	0.915	0.364
Cooling	Flow (LPM)	1.06 ± 0.70	1.28 ± 0.50	-1.416	0.162
	MAP	52.81 ± 13.20	50.06 ± 9.70	0.949	0.346
	ACT (sec.)	754.87 ± 180.36	696.90 ± 187.99	1.259	0.213
	Temp.	27.31 ± 1.98	30.80 ± 2.41	-6.309	**<0.001**
	Lactate	2. 34 ± 1.45	2.32 ± 0.69	0.055	0.956
Rewarming	Flow (LPM)	1.30 ± 0.74	1.42 ± 0.54	-0.793	0.431
	MAP	77.78 ± 100.16	56 ±8 .69	1.225	0.225
	ACT (sec.)	745.28 ± 173.05	682.18 ± 187.30	1.4	0.167
	Temp.	32.33 ± 1.07	33.78 ± 0.92	-5.79	**<0.001**
	Lactate	2.24 ± 1.55	2.47 ± 0.89	-0.729	0.469
Weaning	MAP	63.68 ± 13.26	69.84 ± 11.20	-2.005	**0.049**
	ACT (sec.)	135.73 ± 28.66	152.40 ± 17.67	-2.801	**0.007**
	Temp.	33.55 ± 0.69	34.73 ± 0.81	-6.249	**<0.001**
	Lactate	2.19 ± 1.21	2.66 ± 1.06	-1.652	0.104

During the initiation of cardiopulmonary bypass, the mean CPB Max flows in the "FFP" group was 1.14 ± 0.76 and 1.14 ± 0.76 l/min in the "non-FFP" group. The Mean arterial pressure (MAP) in "FFP group was 42.46 ± 9.12 vs 45.53 ± 9.51 mmHg in "non-FFP" group. The mean activated clotting time (ACT) in "FFP" was 750.12 ± 194.10 vs 631.84 ± 163.29 seconds in "non-FFP" group which was statistically significantly in "FFP" group. The mean temperature in the "FFP" group was 35.19 ± 0.88 vs. 35.65 ± 1.75 degree Celsius in the Non -FFP group. The mean lactate level in the "FFP" group was 2.43 ± 1.30 and 2.17 ± 0.94 mmol/l in the non-FFP group.

During the cooling phase of cardiopulmonary bypass, mean CPB Max. flows in "FFP" group was 1.06 ± 0.70 respectively 1.28 ±

0.50 l/min in the "non-FFP" group. The Mean arterial pressure (MAP) in "FFP group was 52.81±13.20 vs 50.06 ± 9.70 mmHg in Non FFP group. The mean Activated clotting time (ACT) in "FFP" group was 754.87 ± 180.36 and 696.90 ± 187.99 seconds in "non-FFP" group. The mean temperature in the "FFP" group was 27.31 ± 1.98 vs. 35.65 ± 1.75 degree Celsius in the "Non- FFP" group, which was statistically significant. The temperature was maintained moderately hypothermic in fresh frozen plasma group due to complexity of the surgery. The mean lactate level in the FFP group was 2.34 ± 1.45 and 2.32 ± 0.69 mmol/l in the "non-FFP" group.

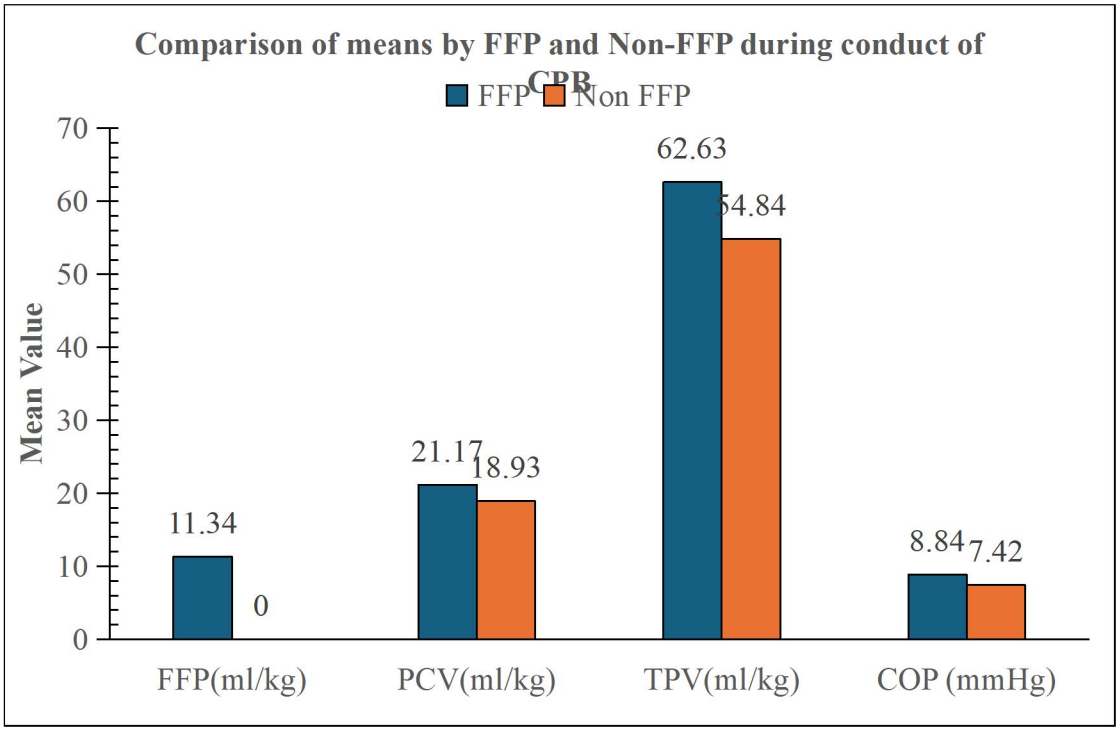
During the Rewarming phase of cardiopulmonary bypass mean CPB max. flows in "FFP" group were 1.30 ± 0.74 respectively 1.42 ± 0.54 l/min in the "Non FFP" group. The Mean arterial pressure (MAP) in the FFP group was 77.78±100.16 vs 56 ± 8.69 mmHg in "non-FFP" group. The mean Activated clotting time (ACT) in "FFP" group was 745.28 ± 173.05 vs 682.18 ± 187.30 seconds in "non-FFP" group. The mean temperature in the "FFP" group was 32.33 ± 1.07 and 33.78 ± 0.92 degree Celsius in the "Non- FFP" group, which was statistically significant. The mean lactate level in the "FFP" group was 2.24 ± 1.55 and 2.47 ± 0.89 mmol/l in the "non-FFP" group.

During the weaning phase of CPB, the Mean arterial pressure (MAP) in the "FFP" group was 63.68 ± 13.26 and 69.84 ± 11.20 mmHg in the "Non FFP" group, which was statistically significant. The mean activated clotting time (ACT) in the "FFP" group was 135.73 ± 28.66 vs 152.40 ± 17.67 seconds in the "non-FFP" group, which was statistically significantly higher in the "Non FFP" group. The mean temperature in the "FFP" group was 33.55 ± 0.69 compared with 34.73 ± 0.81 degree Celsius in the "Non -FFP" group, which was statistically significant. The mean lactate level in the "FFP" group was 2.19 ± 1.21 respectively 2.66 ± 1.06 mmol/l in the "non-FFP" group as seen in table 4.

Table 5. Comparison of Priming Volume Requirement and Circulating Oncotic Pressure In "FFP" and "Non-FFP" Group During Conduct of CPB

Variable	FFP	Non FFP	t value	p value
	Mean ± SD	Mean ± SD		
Fresh frozen plasma (ml/kg)	11.34 ± 4.95	0 ± 0	12.939	**<0.001**
Packed cell volume (ml/kg)	21.17 ± 18.96	18.93 ± 9.71	0.594	0.554
Total priming volume (ml/kg)	62.63 ± 36.46	54.84 ± 24.29	1.006	0.318
Circulating Oncotic pres.(mmHg)	8.84 ± 1.32	7.42 ± 1.56	-1.96021	**0.027**

The mean Fresh Frozen Plasma (FFP) used during priming of cardiopulmonary bypass in "FFP" group was 11.34 ± 4.95 ml/kg against "No-FFP" was used in "non-FFP" group. Thus, the statistical analysis shows significance. The mean Packed Cell Volume (PCV) used in the "FFP" group was 21.17 ± 18.96 contrasted 18.93±9.71 ml/kg in the "non-FFP" group. The mean total priming Volume (TPV) in the "FFP" group was 62.63 ± 36.46 in comparison with 54.84 ± 24.29 ml/kg in the "non-FFP" group. The mean COP in the "FFP" group was 8.84 ± 1.32 vs 7.42 ± 1.56 mmHg in "non-FFP" group which was statically significant higher in "FFP" group due to the use of fresh frozen plasma as seen in table 5 graph 4.



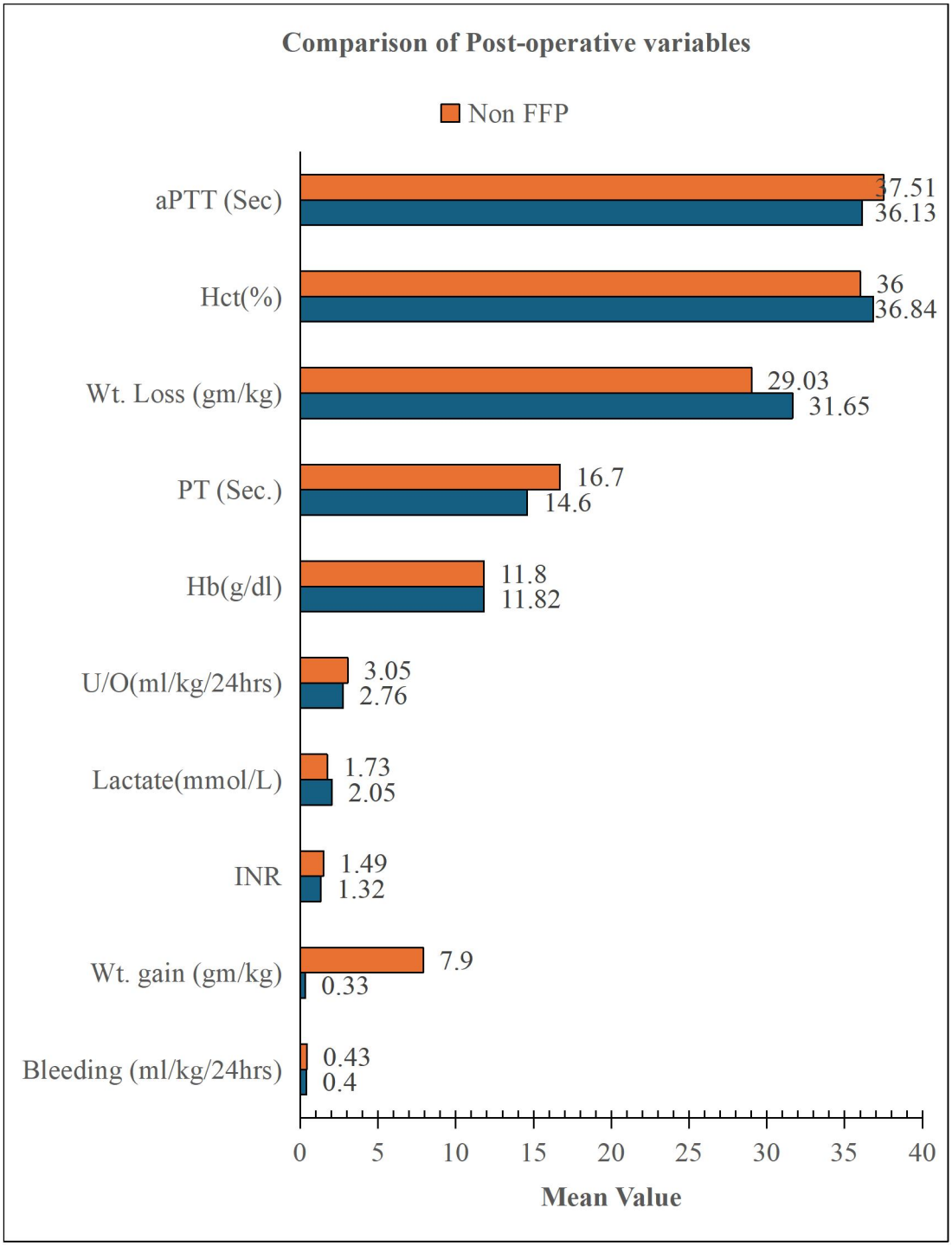
Graph 4. Comparison of Priming volume requirement and Circulating Oncotic Pressure In "FFP" and "Non-FFP" Group During Conduct of CPB

Table 6 Comparison of Post-operative Variables In "FFP" and "Non FFP" Group 24 Hours After Surgery.

Variable	FFP	Non FFP	t value	p value
	Mean ± SD	Mean ± SD		
Bleeding (ml/kg/24hrs)	0.40 ± 0.29	0.43 ± 0.29	-0.298	0.767
Urine Output(ml/kg/24hrs)	2.76 ± 0.91	3.05 ± 1.28	-1.066	0.291
Platelet Count (Plt/µl)	249187.5±98089.63	234906.25±63985.56	0.69	0.493
Lactate (mmol/L)	2.05 ± 2.63	1.73 ± 0.77	0.648	0.519
Hematocrit (%)	36.84 ± 3.91	36.00 ± 6.01	0.66	0.512
Hemoglobin (g/dl)	11.82 ± 1.61	11.80 ± 1.80	0.056	0.955
International Normalized Ratio (INR)	1.32 ± 0.29	1.49 ± 0.33	-2.15	0.034
Prothrombin time (S)	14.60 ± 3.73	16.70 ± 4.36	-2.066	**0.043**
Activated partial Thromboplastin time (aPTT) (S)	36.13 ± 8.38	37.51 ± 4.46	-0.822	0.414

Weight gain (gm/kg)	0.33 ± 1.91	7.9 ± 15.95	-2.661	**0.01**
Weight Loss (gm/kg)	31.65 ± 20.65	29.03 ± 36.05	0.357	0.722

The mean bleeding in the "FFP" group was 0.40 ± 0.29 compared with 0.43 ± 0.29 ml/kg/24hrs in the "non-FFP" group. The mean urine output in the "FFP" group was 2.76 ± 0.91 and 3.05 ± 1.28 ml/kg/24hrs in the "non-FFP" group. The mean platelet count in the "FFP" group was 249187.5 ± 98089.63 respectively 234906.25 ± 63985.56 Plt/µl in the "non-FFP" group. The average lactate level in the "FFP" group was 2.05±2.63 and 1.73±0.77 mmol/L in the "Non- FFP" group. The mean hematocrit in the "FFP" group was 36.84 ± 3.91 versus 36.00 ± 6.01 % in the "non-FFP" group. The mean hemoglobin in the "FFP" group was 11.82 ± 1.61 vs. 11.80 ± 1.80 g/dl in the "non-FFP" group. The mean International normalized ratio (INR) in the "FFP" group was 1.32 ± 0.29 contrasted to 1.49 ± 0.33 in the "non-FFP" group. The mean Prothrombin time (PT) in the "FFP" group was 14.60 ± 3.73 respectively 16.70 ± 4.36 seconds in the "non-FFP" group, which was statically significant high in the "non-FFP" group. The mean activated Partial Thromboplastin Time (aPTT) in the FFP group was 36.13 ± 8.38 and 37.51 ± 4.46 in the "Non FFP" group. The mean weight gain in the "FFP" group was 0.33 ± 1.91 compared with 7.9 ± 15.95 gm/kg in the "non-FFP" group, which was statically significant higher in "non-FFP" group. The mean weight loss in the "FFP" group was 31.65±20.65 compared to 29.03 ± 36.05 gm/kg in the "Non-FFP" group as seen in table 6, graph 5.



Graph 5. Comparison of Postoperative Variables In "FFP" and "Non- FFP" Group 24 Hours After Surgery.

Table 7. Incidence of Complications, Mortality, Re-exploration 24 - Hours After Surgery In "FFP" Vs. "Non FFP" Groups.

Incidence	FFP		Non-FFP		Total (64)
	n (32)	%	n (32)	%	
Complications	2	6.24	4	12.48	0
Re-exploration	0	0	0	0	0 (0)

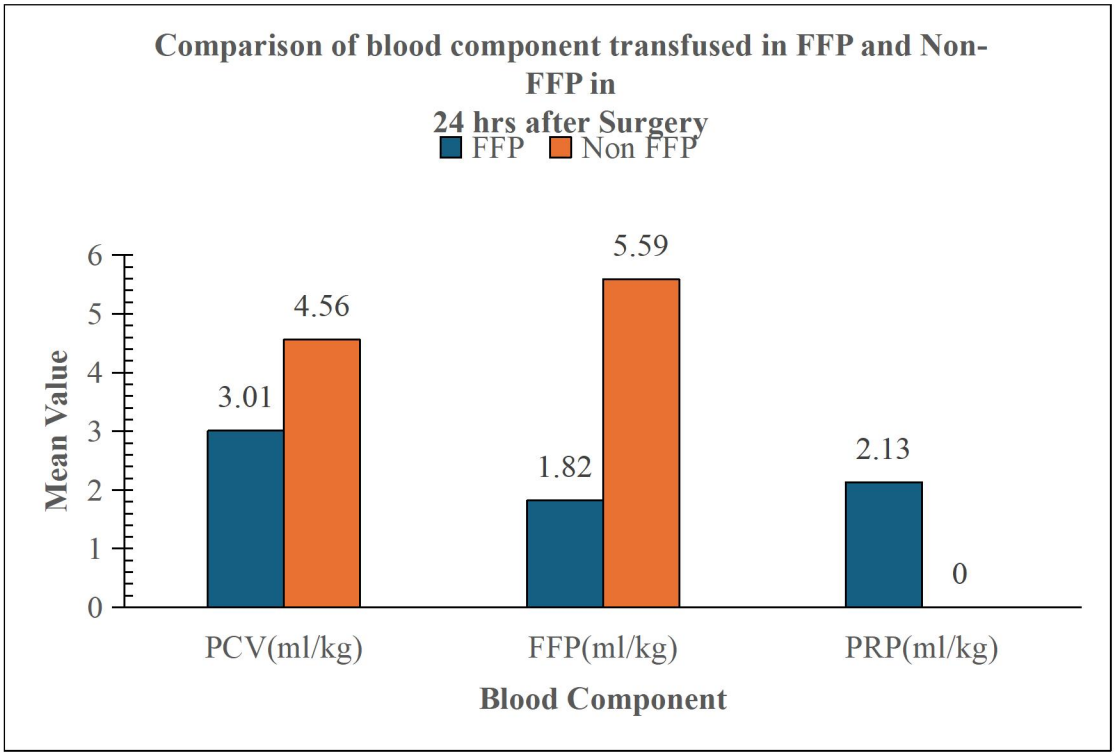
Mortality	2	6.24	0	0	2(6.25)

Morbidity and mortality occurred in 2 (6.24%) in the "FFP" group, and in the non-FFP group, it was nil. Re-exploration and morbidity were nil in both the "FFP" and "Non-FFP". The reason of mortality in one case was cardiopulmonary arrest secondary to severe cardiac failure while other was cardiorespiratory arrest due to fulminant septicaemia. The minor complications such as wound infection occurred in two subjects of FFP group simultaneously four subjects in non-FFP group and some subjects stayed for prolong period in paediatric intensive therapy unit as seen in table 7.

Table 8 Comparison of Blood Products Transfused In "FFP" contrast to "Non FFP" Group in 24 Hours After Surgery.

Variable	**FFP**	**Non FFP**	**t value**	**p value**
	Mean ± SD	**Mean ± SD**		
Packed cell volume (ml/kg)	3.01 ± 7.42	4.56 ± 9.25	-0.739	0.463
Fresh frozen plasma (ml/kg)	1.82 ± 5.02	5.59 ± 10.43	-1.842	**0.07**
Platelet concentrate (ml/kg)	2.13 ± 6.18	0	1.957	**0.055**

The mean Packed cell volume (PCV) used in the "FFP" group was 3.01 ± 7.42 and 4.56 ± 9.25 ml/kg in the "non-FFP" group. The mean Fresh Frozen Plasma (FFP) used in the "FFP" group was 1.82 ± 5.02 respectively 5.59 ± 10.43 ml/kg in the "non-FFP" group, which was statistically significantly higher in the "non-FFP" group. The mean platelet concentrate used in the "FFP" group was 2.13 ± 6.18ml/kg while there was no use of platelet concentrate in "non-FFP" group which was statically significant higher in "FFP" group as seen in table 8, graph 7.



Graph 6. Comparison of Blood Products Transfused In "FFP" contrast to "Non FFP" Group in 24 Hours After Surgery.

Table 9. Comparison of Operations Involved in FFP Vs. Non FFP Group

Operations	FFP (32)		Non FFP (32)		Total (64)	
	n	%	n	%	n	%
Arterial Switch	1	3.1	0	0.00%	1	1.6
ASD Closure	1	3.1	15	46.9	16	25
Atrial Switch	1	3.1	0	0	1	1.6
Atrioventricular Canal Repair	3	9.4	0	0	3	4.7
Fontan Completion	2	6.3	0	0	2	3.1
Intra cardiac repair (ICR)	7	21.9	1	3.1	8	12.5
Main pulmonary artery (MPA) Plasty	1	3.1	0	0	1	1.6
Myxoma Excision	1	3.1	0	0	1	1.6
Total anomalous pulmonary venous connection Repair (TAPVC)	3	9.4	1	3.1	4	6.3
Tricuspid valve (TV) Repair	1	3.1	0	0	1	1.6
Ventricular septal defect (VSD) Closure	11	34.4	13	40.6	24	37.5
AV + MV Repair	0	0	1	3.1	1	1.6

Coronary cameral fistula (CCF) Repair	0	0	1	3.1	1	1.6

The operations involved in “FFP” group was Arterial switch 1(3.1%), ASD Closure 1(3.1%), Atrial Switch 1(3.1%), AV Canal Repair 3(9.4%), Fontan Completion 2(6.3%), Intra Cardiac Repair (ICR) 7(21.9%), MPA Plasty 1(3.1%), Myxoma Excision 1(3.1%), TAPVC Repair 3(9.4%), Tricuspid Valve Repair (TV Repair) 1(3.1%), VSD Closure 11(34.4%).

The operations involved in the “non-FFP” group were ASD Closure 15(46.9%), ICR 1(3.1%), TAPVC Repair 1(3.1%), VSD Closure 13(40.6%), AV+MV Repair 1(3.1%), and Coronary Cameral Fistula (CCF Repair) 1 (3.1%) as seen in table 9.

Discussion

Sixty-four paediatric patients, all under 10 years of age, undergoing elective open-heart surgery with cardiopulmonary bypass (CPB), received fresh frozen plasma ("FFP" group) or without fresh frozen plasma ("non-FFP" group) as part of the CPB prime. The objective of this study was to compare the effects of the "FFP" and "non-FFP" groups on bleeding tendencies, coagulation profiles, urine output, body weight, and biochemical variables, including hemoglobin (Hb), hematocrit (Hct), and platelet count.

We assessed the effects of these priming solutions on circulating oncotic pressure (COP), mean arterial pressure (MAP), hemoglobin, hematocrit, lactate, urine output, bleeding, coagulation profile, and weight changes during and after cardiopulmonary bypass. We also examined the demographic, clinical, and procedural characteristics of both groups. Postoperatively, patients were monitored for bleeding through chest drainage, urine output, biochemical markers, and coagulation profiles. Blood samples were collected 24 hours after surgery for analysis of biochemical variables and coagulation profiles.

Postoperative outcome variables, including blood component transfusions, weight gain or loss, complications, and mortality in the cardiac ICU, were assessed. This included monitoring for body edema, bleeding, coagulation profiles, biochemical markers, and perioperative complications, which were considered in evaluating the patient outcomes. Despite similar age distributions, the "FFP" group exhibited significantly better bleeding tendencies and coagulation profiles.

There wasn’t any noteworthy difference in baseline colloidal oncotic pressure between the groups, but after priming, the “FFP" group had significantly higher circulating colloidal oncotic pressure. This is likely due to the albumin in FFP, which helps prevent fluid shift to the extracellular space and plays a major role in restoring colloidal oncotic pressure. Our findings align with Golab et al[12] who suggested that maintaining high circulating colloidal oncotic pressure reduces fluid shift to the intracellular space, thus decreasing postoperative tissue edema and weight gain.

During the early phase of CPB, the "FFP" group maintained better mean arterial pressure compared to the "non-FFP" group, possibly due to greater hemodilution caused by fresh frozen plasma. However, during the cooling and rewarming phases of CPB, the "FFP" group showed significantly higher mean arterial pressure, likely due to the increased circulating oncotic pressure. At weaning, the "non-FFP" group had greater MAP than the "FFP" group, suggesting that the "non-FFP" group better maintains mean arterial pressure during the early and weaning phases, while the "FFP" group performs better preservation of mean arterial pressure during the cooling and rewarming phases due to physiological changes in fluid due to circulating oncotic pressure.

Despite better mean arterial pressure maintenance in the "FFP" group during the initial and warming phases of CPB, the "non-FFP" group showed higher rates of postoperative bleeding and coagulation abnormalities. This may be due to the lack of anticoagulants like antithrombin III in the "non-FFP" group. Chores BJ et al[9] concluded that maintaining high colloidal oncotic pressure during cardiopulmonary bypass with fresh frozen plasma preserves mean arterial pressure.

The Activated Clotting Time (ACT) was significantly higher at the initiation, cooling, and rewarming phases of cardiopulmonary bypass in the "FFP" group, but post-weaning, ACT was higher in the "non-FFP" group. This suggests that fresh frozen plasma in priming solutions prolongs activated clotting time due to the clotting factors it contains, which enhance heparin activity. After

weaning from CPB, these clotting factors interact with protamine sulfate to reverse the effects of heparin effectively, returning activated clotting time to baseline levels.

The lactate during CPB initiation, cooling and rewarming had not any noticeable change in either group.Postoperative biochemical analysis showed no significant differences in hemoglobin (Hb) and hematocrit (Hct) levels between the groups 24 hours post-surgery. However, the "non-FFP" group required significantly more transfusions of packed red blood cells and FFP compared to the "FFP" group, suggesting that fresh frozen plasma helps to preserve red blood cells and reduce bleeding in the chest drain postoperative. Platelet counts were slightly higher in the "FFP" group after 24 hours, likely due to the preservation of platelets than "non FFP" group. Dieu et al[8] also found that fresh frozen plasma priming in paediatric cardiac surgery resulted in higher platelet counts than non-fresh frozen plasma priming in CPB.

Urine output within 24 hours showed no significant differences between the groups, as both priming solutions had similar effects on renal function. Postoperative coagulation analysis revealed significantly PT, aPTT), and INR levels in the "non-FFP" group, likely due to cardiopulmonary bypass-related protein denaturation and consumption of coagulation factors, which were replenished in the "FFP" group.

Bleeding through the chest drain in the first 24 hours was slightly higher in the "non-FFP" group, and fresh frozen transfusion was significantly higher in this group as well. This suggests that fresh frozen plasma helps preserve haemostasis and reduce postoperative bleeding in chest drain and requirement of blood components transfusions. The "non-FFP" group also experienced greater fluid shift from the intravascular to the extravascular region, which results in significant weight gain.

The incidence of mortality was 6.22% in the "FFP" group. The reason of mortality in one case was cardiopulmonary arrest secondary to severe cardiac failure while other was cardiorespiratory arrest due to fulminant septicaemia. Notably, no patients in either group experienced massive postoperative bleeding, but some patients showed minor complications such as surgical site wound infection and prolonged stay in paediatric ICU. A larger sample size might have helped further validate these findings.

In conclusion, the study found that the "FFP" group required fewer blood component transfusions, had higher platelet counts, experienced weight loss, maintained circulating colloidal oncotic pressure, and demonstrated a normal coagulation profile compared to the "non-FFP" group postoperatively. However, massive bleeding was not observed in either group. Despite the 2 mortalities in the "FFP" group, these were attributed to heart failure and septicaemia not bleeding. Bianchi P et al[10] also reported similar findings, showing that fresh frozen plasma priming in paediatric cardiac surgery is slightly superior to non-FFP priming in cardiopulmonary bypass circuit.

Overall, the study emphasizes the importance of carefully selecting preoperative treatments and monitoring for complications to achieve optimal outcomes. The findings suggest that using FFP as a priming agent in paediatric CPB may improve postoperative outcomes.

Limitation

- The impact of pulsatile and non-pulsatile flows on bleeding was not evaluated and considered for the present study.
- The study failed to evaluate bleeding and other factors by sex.
- The clinical and biochemical parameters were studied only for 24 hours postoperatively; data beyond 24 hours was not considered for the present study, which could have focused on the impact of these different primes more clearly.
- In the present study, we didn't measure colloidal oncotic pressure postoperatively.
- We couldn't match the surgical procedure between the two subgroups.
- We couldn't include the side effects of blood components used in cardiopulmonary bypass and post-operatively.
- The sample size was small.

Recommendation

Based on our experience FFP can be used in patients with complex congenital conditions, cyanotic heart disease, prolong CPB time and less then 10 kg to reduce risk of bleeding and achieve better post operative outcomes in terms of bleeding, better COP etc.

Conclusion

The "FFP" group outperformed the “non-FFP" group in terms of postoperative outcomes, coagulation profile preservation, postoperative blood component transfusion requirements, and maintenance of higher colloidal oncotic pressure. There were no notable bleeding incidents when FFP was added in the prime as opposed to when it wasn't.

BIBLIOGRAPHY

1. Sarkar M, Prabhu V. Basics of cardiopulmonary bypass. Indian journal of anaesthesia. 2017 Sep 1;61(9):760-7.
2. Steen S, inventor; XVIVO Perfusion AB, assignee. Priming solutions for cardiopulmonary bypass. United States patent US 8,969,323. 2015 Mar 3.
3. Ghosh S, Falter F, Perrino AC, editors. Cardiopulmonary bypass. Cambridge university press; 2015 Nov 26.
4. Abedzadeh M, Kachoueian N, Fazli A, Pazhoha M, Omid SO, Vahid P, Givtaj N. The impact of using fresh frozen plasma in cardiopulmonary bypass preparation on thromboelastometric parameters and receiving blood products among pediatric patients undergoing cardiac surgery. Journal of Cardiovascular and Thoracic Research. 2023;15(1):9.
5. Ranucci M, Di Dedda U, Isgrò G, Giamberti A, Cotza M, Cornara N, Baryshnikova E. Plasma-Free Strategy for Cardiac Surgery with Cardiopulmonary Bypass in Infants< 10 kg: A Retrospective, Propensity-Matched Study. Journal of Clinical Medicine. 2023 Jun 7;12(12):3907.
6. Tyagi M, Maheshwari A, Guaragni B, Motta M. Use of Fresh-frozen Plasma in Newborn Infants. Newborn (Clarksville, Md.). 2022 Jul;1(3):271.
7. Fathi M, Hosseinzadeh M, Ivraghi MS, Maleki MH, Jarahi L, Pakniat H, Bakhtiary E, Hasanabad ZA. Assessment of Clinical and Laboratory Outcomes in Using Albumin and Fresh Frozen Plasma as Cardiopulmonary Bypass Prime Solutions in Pediatric Arterial Switch Surgery. Archives of Anesthesia and Critical Care. 2022 Jul 31.
8. Dieu A, Rosal Martins M, Eeckhoudt S, Matta A, Kahn D, Khalifa C, Rubay J, Poncelet A, Haenecour A, Derycke E, Thiry D. Fresh frozen plasma versus crystalloid priming of cardiopulmonary bypass circuit in pediatric surgery: a randomized clinical trial. Anesthesiology. 2020 Jan 1;132(1):95-106.
9. Massoumi G, Mardani D, Mousavian SM, Bigdelian H. Comparison of the effect of fibrinogen concentrate with fresh frozen plasma (FFP) in management of hypofibrinogenemic bleeding after congenital cardiac surgeries: a clinical trial study. ARYA atherosclerosis. 2018 Nov;14(6):248.
10. Bianchi P, Cotza M, Beccaris C, Silvetti S, Isgrò G, Pomè G, Giamberti A, Ranucci M, Surgical and Clinical Outcome REsearch (SCORE) group. Early or late fresh frozen plasma administration in newborns and small infants undergoing cardiac surgery: the APPEAR randomized trial. BJA: British Journal of Anaesthesia. 2017 May 1;118(5):788-96.
11. Balajadia Jr AD. Effects of fresh frozen plasma on post-op bleeding in infants undergoing cardiac surgery with cardiopulmonary bypass (Doctoral dissertation, The University of Arizona).2016 Apr.
12. Golab HD, Scohy TV, de Jong PL, Kissler J, Takkenberg JJ, Bogers AJ. Relevance of colloid oncotic pressure regulation during neonatal and infant cardiopulmonary bypass: a prospective randomized study. European journal of cardio-thoracic surgery. 2011 Jun 1;39(6):886-911
13. McCall MM, Blackwell MM, Smyre JT, Sistino JJ, Acsell JR, Dorman BH, Bradley SM. Fresh frozen plasma in the pediatric pump prime: a prospective, randomized trial. The Annals of thoracic surgery. 2004 Mar 1;77(3):983-7.
14. Chores JB, Holt DW. Colloid oncotic pressure, monitoring its effects in cardiac surgery. The Journal of ExtraCorporeal Technology. 2017 Dec 1;49(4):249-56.
15. Kerkhof AC. Plasma colloid osmotic pressure as a factor in edema formation and edema absorption. Annals of Internal Medicine. 1937 Dec 1;11(6):867-80.