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CORRELATION BETWEEN POST-TRANSFUSION INR AND THE NUMBER OF FRESH FROZEN PLASMA UNITS ADMINISTERED ACROSS DIFFERENT CLINICAL CONDITIONS

Pathology

Dr. Pareena Qureshi	Post Graduate Resident, Department of Pathology, Gandhi Medical College Bhopal
Dr. Jestine K. Abraham	Post Graduate Resident, Department of General Medicine, Gandhi Medical College Bhopal
Dr. Sushil Songara	PGMO Pathology, District Hospital Dewas
Dr. Archana Shrivastava	Associate Professor, Department of Pathology, Gandhi Medical College Bhopal
Dr . Manish Sulya	Professor & Head, Department of Pathology, Gandhi Medical College Bhopal
Dr Chaitra C M*	Post Graduate Resident, Department of Community Medicine, Gandhi Medical College Bhopal *Corresponding Author

ABSTRACT

Background: Fresh Frozen Plasma (FFP) is widely used for the correction of coagulopathy in various clinical settings. However, the effectiveness of FFP in lowering the International Normalized Ratio (INR) and the correlation between the number of units transfused and post-transfusion INR remain subjects of debate. **Aims and Objectives:** This study aimed to evaluate the correlation between post-transfusion INR and the number of FFP units administered across different clinical conditions. The specific objectives were to determine the extent of INR reduction following FFP transfusion and assess its effectiveness across different baseline INR ranges. **Methodology:** A cross-sectional, hospital-based study was conducted in the Department of Pathology at a Tertiary Care Centre of Cental India, from August 1, 2022, to January 31, 2024. A total of 130 patients receiving FFP for coagulopathy correction were included. Pre- and post-transfusion INR values and the number of FFP units transfused were recorded. Statistical analysis was performed using SPSS software, with Pearson's correlation coefficient used to assess relationships between variables. **Results:** FFP transfusion led to a significant INR reduction in 68% of patients, with an average decrease of 1.2 ± 0.3 units. Patients with pre-transfusion INR >2.5 experienced the greatest reduction (≥30% in 75% of cases), whereas those with INR between 1.5 and 2.0 showed a modest decline of 0.5 ± 0.2 units. A weak positive correlation (r=0.32, p=0.04) was found between the number of FFP units administered and the extent of INR correction, indicating diminishing returns with excessive transfusions. **Conclusion:** FFP transfusion is most effective in patients with severe coagulopathy (INR >2.5), with limited benefit observed in those with mild INR elevations. The findings emphasize the need for targeted transfusion practices to optimize FFP utilization and minimize unnecessary transfusions.

KEYWORDS

FFP, INR, Post Transfusion, correlation

INTRODUCTION

Fresh Frozen Plasma (FFP) is an essential blood component frequently used in clinical practice for the management of coagulation disorders, liver dysfunction, massive transfusions, and various bleeding conditions. [1] It serves as a critical source of coagulation factors, including fibrinogen, prothrombin, and factors V, VII, VIII, IX, X, and XI, which are necessary for hemostasis. FFP is primarily administered to correct prolonged prothrombin time (PT) and International Normalized Ratio (INR) to reduce the risk of bleeding complications in patients with coagulation abnormalities. [2] However, the response to FFP transfusion is highly variable and influenced by multiple factors, including the underlying clinical condition, baseline coagulation status, and the number of plasma units transfused. [3]

INR is a standardized parameter widely used to assess coagulation status and guide FFP transfusion decisions. The expectation is that FFP transfusion will lower INR in patients with coagulopathy; however, the extent of INR correction is not uniform across all patient populations. Research suggests that pre-transfusion INR levels, patient age, liver function status, and disease etiology significantly impact the degree of INR reduction. Generally, patients with markedly elevated pre-transfusion INR experience a more significant decrease in INR following FFP administration, whereas those with only mildly prolonged INR often show minimal or no meaningful reduction. [4] [5]

Despite its widespread use, there is ongoing debate regarding the optimal threshold for FFP transfusion and its actual clinical benefit, especially in non-bleeding patients. [6] The indiscriminate use of FFP in cases of mildly elevated INR remains a concern, as it may contribute to unnecessary transfusions without significantly altering coagulation status. [7] Moreover, the correlation between the number of FFP units administered and the extent of INR correction is not well established across different clinical scenarios.[8] This study aims to assess the relationship between post-transfusion INR and the number of FFP units administered in various clinical conditions. By evaluating this correlation, we seek to refine transfusion guidelines, improve FFP utilization, and promote evidence-based practices that enhance patient safety while minimizing unnecessary blood product use.

MATERIALS AND METHODS

Study Design

This was a cross-sectional, hospital-based study conducted in the Department of Pathology at a tertiary care centre at Central India, from August 1, 2022, to January 31, 2024. The study aimed to evaluate the correlation between post-transfusion INR and the number of Fresh Frozen Plasma (FFP) units administered across different clinical conditions.

Study Population

The study included patients who received FFP transfusion for various clinical indications, including coagulopathies, liver dysfunction, and massive transfusions. Patients were selected based on their medical records and INR measurements before and after transfusion.

Inclusion Criteria

- Patients who received FFP transfusion for correction of coagulopathy.
- Patients with available pre- and post-transfusion INR values.
- Patients who provided informed consent.

Exclusion Criteria

- Patients who received additional blood products (e.g., platelets, cryoprecipitate) during the same transfusion episode.
- Patients with underlying conditions that could independently alter INR values (e.g., disseminated intravascular coagulation, anticoagulant overdose).
- Patients with incomplete medical records or missing INR values.

Sample Size

A total of 130 patients who received FFP transfusions at the hospital from August 1, 2022, to January 31, 2024, were included in the study.

Data Collection

Informed consent was obtained from all participants, and confidentiality of patient data was strictly maintained. The values of both pre-transfusion and post-transfusion INR was recorded in the MS Excel sheet and the difference was calculated. Prothrombin time was tested by manual method (Quick's method)

INR= (PT of patient ÷ PT of control)^{ISI}, where ISI is International Sensitivity Index of thromboplastin reagent, which is provided by its manufacturer. ISI value of the reagent used was 1.2.

The change in INR per unit of FFP transfused was calculated. Relationship between the pre-transfusion INR and improvement in the INR per unit of FFP was studied using Pearson's correlation. The number of patients who showed significant improvement in the INR was determined using the following formula derived by Holland and Brooks. Significant change is ≥8.9% of pre-transfusion INR. A change in INR per unit of FFP greater than or equal to 8.9% of the pre transfusion INR was considered as significant as per the formula derived by Holland and Brooks. INR>1.5 was considered as deranged and only those patients with INR>1.5 were included in the study. The patients were categorised into two cohorts: one with INR 1.5-3 as mild to moderate coagulation defect and the other with INR>3 were considered as severe coagulation defect. Data were extracted from electronic medical records and transfusion logs.

Statistical Analysis

Data were entered into Microsoft Excel and analyzed using SPSS software. Descriptive statistics, including mean, standard deviation, and percentages, were used. The correlation between the number of FFP units transfused and post-transfusion INR was assessed using Pearson's correlation coefficient. Group comparisons were conducted using the chi-square test for categorical variables and t-test for continuous variables, with a significance threshold of $p<0.05$.

RESULTS

Total 126 patients receiving FFP and fulfilling the inclusion criteria were included in our study. Out of these, 20 subjects were under the age of 1 year who received FFP less than 1 unit. These cases were studied separately. 1 standard unit of FFP was considered 175ml. 6/106 (5.66%) patients were between 1 year and 14 years comprising the pediatric population while 100/106 (94.33%) were over 14 years of age. Mean age of patients receiving FFP transfusion was 35 years. Out of the total subjects, 53/106 (50%) were males and 53/106 (50%) were females. 5.66% were 1- 14 year of age group and 94.33% were > 14 year of age group

Table 1 : Effect of FFP on INR

INR	N	Mean INR	Range	Std. Deviation	p-value (Paired T- test)
Pre-Transfusion INR	106	2.14	5.39	0.92	0.000*
Post Transfusion INR	106	1.46	2.60	0.35	

* : significant

The mean INR significantly reduced from 2.14 ± 0.92 (range 1.5-6.89) to 1.46 ± 0.35 (0.9-3.5) after FFP transfusion which is statistically significant. (Table 1) Mean FFP units transfused was 3.37 per patient. The mean improvement in INR per unit of FFP was 0.20. According to the formula derived by Holland and Brooks, 37/106 patients (35%) showed significant improvement and 69/106 (65%) did not show significant improvement.

Table 2 : Correlations Between Pre-transfusion INR and Change in INR per unit of FFP

		change in INR per unit of FFP
Pre-Transfusion INR	Pearson Correlation test	.838**
	P-Value	0.000*
	N	106

There is positive Correlation between pre-transfusion INR and change in INR per unit of FFP (Pearson's correlation coefficient r=0.83). (Table 2) This means that higher the pre-transfusion INR, more is the change in INR per unit of FFP post-transfusion.

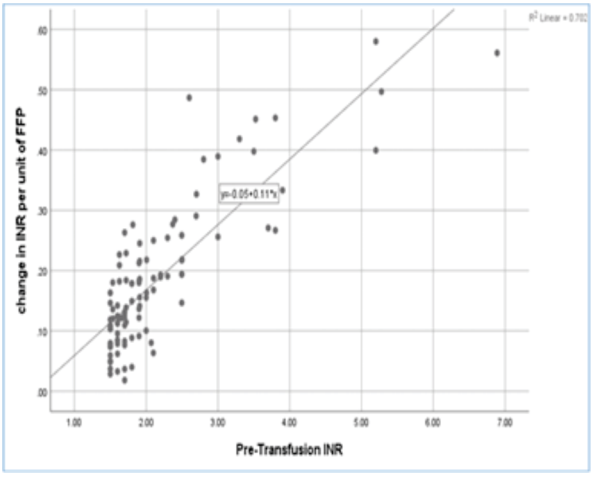

Figure 1 : Correlation Between Pre-transfusion INR and INR Change per unit of Fresh Frozen Plasma (FFP)

Table 3 : Effect of FFP on INR According to Age

Age group	N	Quantity of FFP transfused (in units)	Pre- Transfusion INR	Post Transfusion INR	Net Change in INR	Change in INR per unit of FFP	% change per units of FFP	P-Value Paired t test
		Mean	Mean	Mean	Mean	Mean	Mean	
1-14 year	6	2.50	1.88	1.51	0.36	0.16	7.89%	0.040*
> 14 year	100	3.43	2.15	1.45	0.69	0.20	9.35%	0.000*

* : significant

Table 3 shows that the mean INR significantly reduced in both the age groups, which is statistically significant in both the groups. But reduction is more in >14 age group (net change in INR =0.69) as compared to 1-14 year of age group (net change in INR=0.36).

In the 1–14 years age group, the per-unit change in pre-transfusion INR was 7.89%, which is not significant based on the formula by Holland and Brooks. In contrast, for individuals above 14 years, the change was 9.35%, meeting the significance threshold defined by Holland and Brooks. According to their formula, a decrease of ≥8.9% in pre-transfusion INR per unit of FFP transfused is considered significant

Table 4 : Effect of FFP on INR According to their Pre transfusion INR Status

INR	N	No. of FFP unit transfused (mean)	Mean Pre-Transfusion INR	Mean Post Transfusion INR	Mean change in INR per Unit of FFP	Change in INR per unit of FFP (%)	p-value (paired T test)
1.5- 3 INR	94	292 (3.11)	1.86	1.38	0.1538	7.96	0.000*
>3 INR	12	66 (5.50)	4.30	2.04	0.4133	9.79	0.000*

Out of 106 subjects included in our study, 94 (88.6%) patients had pre-transfusion INR value between 1.5-3.0 with mean pre-transfusion INR 1.86 and 12 patients had pre-transfusion INR>3 with a mean pre-transfusion INR 4.30.(Table 4) Statistical significance was seen in both the groups. However, there was no significant change in INR group 1.5-3.0 as per Holland and Brooks formula (<8.9% change in INR per unit of FFP).

Table 5 : Percentage Change in INR with Respect to their Pre transfusion INR

Pre-transfusion	Change in INR>8.9% per unit of FFP		Change in INR<8.9% per unit of FFP		Total
INR group	n	%	n	%	
1.5- 3 INR	28	29.79%	66	70.21%	94
>3 INR	8	66.67%	4	33.33%	12
TOTAL	36	33.96%	70	66.04%	106

Among the 94 patients with a pre-transfusion INR of 1.5–3.0, only 28 (29.78%) exhibited a significant improvement per unit of FFP, as defined by the Holland and Brooks formula (>8.9%). In contrast, of the 12 patients with a pre-transfusion INR greater than 3.0, 8 (66.67%)

demonstrated a significant reduction per unit of FFP based on the same criteria. (Table 5)

Table 6 : Effect of FFP on INR According to Clinical Conditions

DIAGNOSIS	N	Quantity of FFP transfused (Mean)	Pre-Transfusion INR (Mean)	Post Tansfusion INR (Mean)	Net Change in INR (Mean)	change in INR Per unit of FFP (Mean)	% change (Mean)	P-VALUE
Chronic liver disease	23	4.00	2.78	1.61	1.17	0.25	8.60 %	0.000*
Eclampsia / Pre- eclampsia	18	3.00	1.68	1.35	0.33	0.13	7.71 %	0.000*
Acute liver disease	10	4.00	3.07	1.65	1.42	0.34	10.9 %	0.001*
Cellulitis and sepsis	7	3.00	2.06	1.50	0.57	0.18	9.04 %	0.001*
DIC	6	3.00	1.91	1.38	0.53	0.21	10.81%	0.003*
Carcinoma	5	2.00	1.72	1.32	0.41	0.16	8.83 %	0.027*
Perforation peritonitis	5	3.00	1.76	1.39	0.37	0.11	5.68 %	0.054
Cholecystitis with cholelithiasis	4	4.00	2.22	1.54	0.69	0.19	8.60 %	0.01*
Post-operative bleeding	4	4.00	1.71	1.20	0.51	0.14	8.02 %	0.007*
Chronic kidney disease	3	2.00	1.60	1.29	0.31	0.14	8.69 %	0.013*
* : significant								

Maximum number of FFP units were prescribed for patients with chronic liver disease (23) followed by eclampsia/pre- eclampsia (18), acute liver disease (10), cellulitis and sepsis (7), Disseminated intravascular coagulation (6), various carcinomas (5), perforation peritonitis (5), post-operative bleeding (4) among the major ones. Change in INR after FFP transfusion was found statistically significant (p value<0.05) in all conditions except perforation peritonitis (p value=0.054).(Table 6)

According to formula derived by Holland and Brooks, significant reduction in INR per unit of FFP (≥8.9% of pre-transfusion INR) was seen in cases of acute liver disease, disseminated intravascular coagulation and cellulitis and sepsis whereas the change was not significant (<8.9% reduction in pre-transfusion INR value per unit of FFP) in all other cases.

DISCUSSION

This study evaluated the correlation between post-transfusion INR and the number of FFP units administered across different clinical conditions. The results indicate that while FFP transfusion significantly reduced INR levels, the extent of correction varied depending on the initial INR and underlying clinical condition.

In our study done on 106 patients aged more than 1 year, 5.66% (n=6) cases were of 1- 14 year of age group and 94.33% (n=100) cases were > 14 year of age group with mean age of 35 years. The mean INR reduced from 2.14 ± 0.92 (range 1.5-6.89) to 1.46 ± 0.35 (0.9-3.5) after FFP transfusion (n=106). This difference was statistically significant. These findings align with previous studies. Holland et al.[9] reported a mean INR reduction of 1.1 in patients with baseline INR >2.0, while those with INR between 1.3 and 1.6 had minimal correction (0.2–0.3 units). Similarly, Dzik et al. [10] emphasized that FFP is most effective in cases of severe coagulopathy but provides limited benefit when baseline INR is near normal. Abdel-Wahab et al. [11] found that only 15% of patients with an initial INR of 1.5-1.9 had a meaningful INR reduction, reinforcing the limited efficacy of FFP in patients with mild coagulopathy.

Our study has closest resemblance with that done by Kulkarni et al [12] and Nagulan et al [13] in terms of significance as per formula derived by Holland and Brooks. FFP is often transfused to non-bleeding patients to correct abnormal coagulation tests in an assumption that it will limit the risk of clinical bleeding. This study found a weak positive correlation (r=0.32, p=0.04) between the number of FFP units transfused and the extent of INR reduction, suggesting a threshold effect beyond which additional FFP does not significantly enhance coagulation correction.

Abdel-Wahab et al. [11] studied plasma recipients from a wide variety of hospital wards. In their retrospective study, 324 FFP units were given to 121 patients who had relatively lower pre-transfusion INRs, 1.1–1.85. Very small median reductions in post-transfusion INR was seen 0.07. Those with higher INRs (1.5–1.85) were more likely to correct their coagulation parameters in comparison to those with lower INRs (1.1–1.5). In the study done by Nisha Lekshmy et al [14] on 66 patients, 42 having mild to moderately prolonged pre-transfusion INR (INR<2) showed a change of 0.19 in INR per unit of FFP while per unit change in INR was 0.7 in 24 cases having severely prolonged pre-transfusion INR (>3). The difference between both groups was statistically significant (p value=0.000). They found a linear correlation between the pre-transfusion INR and the improvement in INR post transfusion (Pearson correlation value, r=0.929).

Shinagare et al [15] found a linear relationship between pre-transfusion INR and improvement in INR per unit of FFP (Pearson's correlation coefficient, r=0.89) which was also observed in our study (Pearson's correlation coefficient r=0.83). Holland and Brooks studied 103 adult patients in which mean pre transfusion INR was 2.2 and mean INR post FFP transfusion was 1.5 with a mean change in INR of 0.7. [16] They found that 50% of adult patients with pre-transfusion INR of 1.8 showed significant change per unit of FFP transfused while 38% patients showed significant change when cut off INR was 1.5. They concluded that in adults as well as pediatric population, normalization of INR is minimal in patients with pre-transfusion INR less than 1.7. Segal et al [8] further evaluated the patients undergoing invasive procedures with normal and abnormal PT/INR. On conducting 24 observational studies and one clinical trial, they concluded no statistical significance in the association of raised coagulation parameters and risk of bleeding in patients undergoing kidney biopsy, liver biopsy, central vein cannulation, and others.

In our study, we categorized patients into two cohorts based on pre-transfusion INR. The first cohort (88.6%, n=94) had a mean INR of 1.86 (range: 1.5–3.0), indicating mild to moderate coagulation defects, while the second cohort (n=12) had a mean INR of 4.30 (>3.0), indicating severe coagulation defects. The mean INR change per unit of FFP was 0.15 in the first cohort and 0.40 in the second, both showing statistical significance (p<0.05). According to the Holland and Brooks formula, the change in INR was significant only in the second cohort (9.79% vs. 7.9%). This aligns with studies by Abdel-Wahab et al. [11] , Raturi et al. [17] and Sasikala et al. [18], which reported greater INR reduction in patients with higher pre-transfusion INR. We also observed a strong linear correlation (r=0.83) between pre-transfusion INR and INR reduction, consistent with previous research.

Sukanya Baruah et al.[5] observed that FFP transfusion improved INR more in acute than chronic liver disease, with an average INR improvement of 0.27 per unit. Kulkarni et al[12] reported maximum FFP use in DIC, followed by bleeding and liver disease, while Shinagare et al[15] noted a similar trend, also including hypovolemia and sepsis. Raturi et al.[17] found that FFP was mostly transfused for bleeding, followed by hypovolemia, with a significant INR reduction ($p < 0.001$) and the highest mean INR drop per transfusion episode in bleeding cases (0.41) compared to coagulopathy without bleeding (0.34). In clinical practice, these results highlight the importance of judicious FFP use, targeting patients with significantly elevated INR rather than routine transfusions for mild coagulopathy. This study suggests that transfusions should be prioritized for patients with INR >2.5 to maximize benefit. Further prospective studies with larger cohorts are needed to refine transfusion guidelines and optimize FFP utilization while minimizing unnecessary transfusions.

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