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Original Research Article

Usage of Fresh Frozen Plasma in Chronic Liver Diseases with Clinical Bleeding Diathesis and Its Effect on Prothrombin Time and International Normalized Ratio in Post-Transfusional State

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Abstract

Background: Coagulopathy is a common and clinically significant complication of chronic liver disease (CLD), resulting from impaired hepatic synthesis of clotting factors. Fresh Frozen Plasma (FFP) is widely used to correct these abnormalities, yet its effectiveness in improving coagulation parameters and controlling clinical bleeding remains incompletely characterised in Indian tertiary settings.

Aim: To evaluate the effect of FFP transfusion on Prothrombin Time (PT) and International Normalised Ratio (INR) in adult patients with CLD presenting with clinical bleeding diathesis, and to assess bleeding control outcomes in relation to disease severity.

Methods: A single-centre, hospital-based, pre–post interventional study was conducted at Fakhruddin Ali Ahmed Medical College and Hospital (FAAMCH) (Former name) , but now presently known as Barpeta Medical College and Hospital (BMCH) (After name change of the College and Hospital) , Barpeta, Assam over 18 months. One hundred adult patients with diagnosed CLD, elevated PT and INR, and clinical bleeding diathesis were enrolled. PT and INR were measured before and after FFP transfusion using an automated coagulation analyser. Bleeding control was assessed clinically. Disease severity was graded by the Child–Pugh classification. Data were analysed using paired t-test and chi-square test; $p<0.05$ was considered significant.

Results: Mean PT decreased significantly from 27.8±6.21 seconds pre-transfusion to 20.5±5.78 seconds post-transfusion ($p<0.001$), a mean percentage reduction of 26.5±11.3%. Mean INR declined from 3.77±1.33 to 3.0±1.31 ($p=0.004$), representing a 22.2±12.1% reduction. Bleeding was controlled in 84% of patients; 16% showed no improvement. The majority (76%) were classified as Child–Pugh Class C. Patients with more advanced disease required more FFP units and showed comparatively less consistent bleeding control, though the difference between Class B and Class C was not statistically significant ($p=0.919$).

Conclusion: FFP transfusion produces statistically significant improvements in PT and INR in CLD patients with bleeding diathesis, and supports clinical haemostasis in most cases. However, the degree of benefit is influenced by underlying disease severity, and complete correction is rarely achieved in advanced disease. Routine monitoring of coagulation parameters and judicious use of FFP remain essential in this patient group.

Keywords: Fresh Frozen Plasma, Chronic Liver Disease, Coagulopathy, Prothrombin Time, International Normalised Ratio, Bleeding Diathesis, Child–Pugh Classification.

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Introduction

Chronic liver disease (CLD) encompasses a spectrum of hepatic disorders resulting from persistent injury, including viral hepatitis, alcoholic liver disease, and non-alcoholic fatty liver disease. As the disease progresses, the functional hepatocyte mass declines, impairing two critical haemostatic roles of the liver: synthesis of coagulation factors and clearance of activated clotting components [1]. The resulting coagulopathy is complex, involving simultaneous deficiencies in procoagulant factors (II, V, VII, IX, X) and anticoagulant proteins (protein C, protein S, antithrombin), creating a rebalanced but fragile haemostatic state that is prone to both bleeding and

thrombosis [2]. Clinically, patients with CLD frequently present with bleeding diathesis, including gastrointestinal haemorrhage, mucosal bleeding, bruising, and prolonged bleeding after minor procedures. Prothrombin Time (PT) and the International Normalised Ratio (INR) are the most commonly used laboratory surrogates of hepatic synthetic function and are central to clinical scoring systems such as the Child–Pugh and MELD scores [3]. Elevation of these markers reflects the degree of factor deficiency and guides transfusion decisions.

Fresh Frozen Plasma (FFP) is the most widely administered blood product for correcting coagulopathy in CLD. It contains the full complement of coagulation factors, including labile factors V and VIII, and acts by temporarily replenishing clotting proteins in the circulation [4]. However, the clinical evidence supporting its routine use in this setting is inconsistent. Several studies describe only partial or transient improvement in PT and INR following FFP infusion, with responses that vary according to baseline severity, volume transfused, and the degree of hepatic impairment [5,6]. Additionally, risks of transfusion-related complications, including Transfusion-Related Acute Lung Injury (TRALI) and Transfusion-Associated Circulatory Overload (TACO), must be weighed against potential benefit [7].

In Indian tertiary hospitals, particularly in Northeast India, the aetiology and clinical profile of CLD differ from Western populations—with a high burden of alcohol-related liver disease and hepatitis B—which may influence the haemostatic response to FFP. Local data on the pre- and post-transfusion changes in PT and INR in this context remain limited. The present study was therefore undertaken to systematically evaluate the effect of FFP on PT and INR in patients with CLD presenting with clinical bleeding diathesis at a tertiary care centre in Assam, and to examine the relationship between disease severity and transfusion outcome.

Methodology

Study Design and Setting: A single-centre, hospital- based, pre–post interventional study was conducted in the Department of Pathology at Fakhruddin Ali Ahmed Medical College and Hospital (FAAMCH) (Former name) , but now presently known as Barpeta Medical College and Hospital (BMCH) (After name change of the College and Hospital) , Barpeta , Assam—a tertiary care institution serving a predominantly rural population in lower Assam. The study was carried out over a period of 18 months. Ethical clearance was obtained from the Institutional Human Ethics Committee (IHEC), FAAMCH (Former name), but now presently known as Barpeta Medical College and Hospital (BMCH) ,Barpeta , Assam and written informed consent was obtained from all participants prior to enrolment.

Study Population: A total of 100 adult patients (≥18 years) diagnosed with chronic liver disease were included. Diagnosis of CLD was established clinically, biochemically, and radiologically by the Department of Medicine. Inclusion criteria required: confirmed CLD, elevated PT and INR above the laboratory reference range, and the presence of clinical bleeding diathesis (defined as active or recent spontaneous or trauma-related bleeding including gastrointestinal bleeding, mucosal bleeding, haematuria, or abnormal bruising). Patients receiving anticoagulant medications (heparin, warfarin), those with primary haematological bleeding disorders, acute-on-chronic liver failure with renal shutdown, or those unwilling to participate were excluded. Each participant served as their own control; no separate control group was used. Disease severity was graded according to the Child–Pugh scoring system into Class B and Class C.

Sample Collection and Processing: Five millilitres of venous blood was collected under aseptic precautions in sodium citrate vacutainers. Samples were processed within two hours of collection in accordance with standard laboratory protocols. PT and INR were measured using the Automated Coagulation Analyser ERBA ECL 760 before FFP transfusion and again within 4–6 hours after completion of transfusion. Reference ranges used were: PT 11–13 seconds and INR 0.8–1.2.

FFP Transfusion Protocol: FFP was administered as clinically directed by the treating physician, based on the severity of bleeding and coagulation abnormalities. The number of FFP units transfused per patient was recorded. Bleeding control was assessed clinically by the treating team as achieved (cessation of active bleeding) or not achieved within 24 hours of transfusion.

Statistical Analysis: Data were entered in Microsoft Excel and analysed using SPSS version 21.0. Continuous variables were expressed as mean ± standard deviation (SD). Paired t-test was used to compare pre- and post-transfusion PT and INR values. The chi-square test was applied to compare proportions between subgroups. Pearson correlation was used to examine relationships between continuous variables. A p-value <0.05 was considered statistically significant.

Results and Discussion

A total of 100 patients with CLD and clinical bleeding diathesis were enrolled. The demographic and clinical profile of the study population is summarised below.

Demographic and Clinical Profile: The majority of participants were in the 51–60 year age group (34.00%), followed by the 41–50 year group (25.00%) and 61–70 year group (22.00%). A clear male predominance was observed, with 84 males (84.00%) and 16 females (16.00%).

This distribution is consistent with the known epidemiology of alcohol-related CLD, which disproportionately affects middle-aged males [8]. History of alcohol consumption was present in 79% of participants, reflecting the dominant aetiological contribution of alcohol in this geographic region. Normal BMI was recorded in 44% of participants, while 35% were overweight and 21% were underweight—the latter group reflecting nutritional compromise associated with advanced hepatic dysfunction. Comorbid conditions (diabetes mellitus and hypertension) were present in 44% of patients.

Disease severity stratification showed that 76% of participants were classified as Child–Pugh Class C, while the remaining 24% were Class B. No patients were in Class A, indicating that the study cohort represented a population with predominantly advanced liver disease—the group most likely to require FFP transfusion in clinical practice.

Effect of FFP on Prothrombin Time and INR: Table 1 presents the pre- and post-transfusion values of PT and INR for the entire cohort. The mean PT decreased significantly from 27.8±6.21 seconds before transfusion to 20.5±5.78 seconds after transfusion (paired t-test, $p<0.001$), corresponding to a mean percentage reduction of 26.5±11.3%. Similarly, the mean INR decreased from 3.77±1.33 to 3.0±1.31 ($p=0.004$), a mean reduction of 22.2±12.1%. Both changes were statistically significant, demonstrating that FFP transfusion produces measurable improvements in coagulation parameters in this population.

Table 1: Changes in Prothrombin Time and INR Following FFP Transfusion (n=100)

Parameter	Pre-transfusion (Mean ± SD)	Post-transfusion (Mean ± SD)	% Change (Mean ± SD)	P-value
PT (seconds)	27.8 ± 6.21	20.5 ± 5.78	−26.5 ± 11.3	<0.001*
INR	3.77 ± 1.33	3.0 ± 1.31	−22.2 ± 12.1	0.004*

[*Statistically significant]

These findings are consistent with previous studies examining the effect of FFP in CLD. Baruah et al. (2018) demonstrated significant reduction in PT and INR following FFP transfusion in cirrhotic patients [9]. Similarly, Kapse et al. (2020) reported comparable improvements in coagulation tests post-FFP in patients with decompensated liver disease [10]. However, it is noteworthy that despite statistically significant improvements, the mean post-transfusion INR (3.0±1.31) remained substantially above the normal reference range (0.8–1.2), confirming that FFP achieves partial rather than complete correction of coagulopathy in CLD—a finding that aligns with the inherent limitation of FFP's intrinsic INR (~1.0) limiting its corrective capacity when the patient's pre-transfusion INR is markedly elevated [6].

Bleeding Control Outcomes: Clinical bleeding was controlled in 84 patients (84%), while 16 patients (16%) showed no improvement following FFP transfusion. This rate of bleeding control is in keeping with reports from comparable clinical settings. The inability to achieve haemostasis in 16% of cases likely reflects the multifactorial nature of bleeding in CLD, where platelet dysfunction, portal hypertension-related variceal haemorrhage, and hyperfibrinolysis may contribute alongside coagulation factor deficiency—processes that FFP alone cannot address [2,5].

Coagulation Parameters by Child–Pugh Classification: Table 2 shows the baseline and post-transfusion coagulation values stratified by Child–Pugh class. Patients classified as Child–Pugh Class C had significantly higher baseline PT (30.08±5.30 seconds) and INR (4.25±1.16) compared to Class B patients. Although both groups showed improvement following FFP transfusion, post-transfusion values remained higher in the Class C group, reflecting the more profound synthetic failure in advanced disease. Patients with Class C disease also required a greater number of FFP units to achieve any measurable correction.

Table 2: Coagulation Parameters by Child–Pugh Classification

Parameter	Child–Pugh Class B (n=24) (Mean ± SD)	Child–Pugh Class C (n=76) (Mean ± SD)
PT Pre-transfusion (sec)	22.50 ± 5.10	30.08 ± 5.30
PT Post-transfusion (sec)	17.20 ± 4.80	21.60 ± 5.10
INR Pre-transfusion	2.90 ± 0.95	4.25 ± 1.16
INR Post-transfusion	2.30 ± 0.88	3.30 ± 1.20

[Values are mean ± SD; Class C patients had significantly higher baseline values ($p<0.001$)]

Although bleeding control was achieved in a higher proportion of Class B patients compared to Class C (91.7% vs 81.6%), this difference was not statistically significant (chi-square test, p=0.919). The absence of significance despite the numerical difference may reflect the relatively small sample of Class B patients (n=24) compared to Class C (n=76). This finding supports the clinical observation that response to FFP is inconsistent in advanced disease, and underscores the need for individualized, severity-guided transfusion strategies rather than blanket protocols.

Number of FFP Units and Disease Severity: Patients with Child–Pugh Class C disease received a greater mean number of FFP units compared to Class B patients. This likely reflects the greater degree of factor deficiency in advanced disease, requiring larger volumes of plasma to achieve even partial correction. However, as noted above, larger volumes carry increased risks of circulatory overload and TACO, particularly in patients with pre-existing portal hypertension and fluid retention [7]. These findings reinforce the importance of using viscoelastic tests such as thromboelastography (TEG) or rotational thromboelastometry (ROTEM), where available, to guide more targeted FFP use—an approach now advocated by major haematological societies [11].

Limitations: This study was single-centre and observational, limiting causal inference. The absence of a control group (patients receiving no FFP) precludes direct comparison of the natural trajectory of coagulation parameters without intervention. The pre–post design does not account for the possibility that some improvement in coagulation may have occurred independent of FFP due to other concurrent supportive care.

The timing of post-transfusion sampling (4–6 hours) captures only the immediate haemostatic effect; the transient nature of FFP benefit over 24–48 hours could not be assessed. Additionally, factors such as dietary intake, hepatotoxic medication use, and the specific aetiology of CLD were not fully adjusted for in the analysis. Larger, multi-centre, randomised controlled studies are needed to confirm these findings and to optimise FFP dosing protocols in this population.

Conclusion

The present study demonstrates that FFP transfusion leads to statistically significant improvements in PT and INR in patients with chronic liver disease presenting with clinical bleeding diathesis. Bleeding was controlled in 84% of patients, confirming the clinical utility of FFP in the acute haemostatic management of CLD. However, complete correction of coagulopathy was rarely achieved, and patients with more advanced disease (Child–Pugh Class C) exhibited comparatively greater residual coagulopathy and required higher transfusion volumes. The response to FFP varies with the severity of hepatic dysfunction, and clinicians should not rely solely on laboratory normalisation as an endpoint. These findings highlight the need for systematic coagulation monitoring in CLD patients, region-specific haemostatic data to guide clinical practice, and future investigation into more targeted approaches—including viscoelastic haemostatic assays—to optimise FFP use and reduce transfusion-related risk in this vulnerable population.

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