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# ORIGINAL RESEARCH

## To study the therapeutic efficacy of Fresh Frozen Plasma in cirrhotic patients with low Prothrombin Index (PTI)

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***ABSTRACT***:
**Introduction**: Cirrhosis of liver is a growing cause of significant morbidity and mortality of modernization. Cirrhosis patients have a disturbed balance between procoagulant and anti-coagulant factors and a very poor reserve of these factors leads to increased bleeding risk as well as increased thrombotic risk. **Aim**: To study the therapeutic efficacy of fresh frozen plasma(FFP) transfusion in cirrhotic patients with low prothrombin index and clinical profile of cirrhotic patients before and after FFP transfusion especially with regards to bleeding tendencies. **Material and Methods:** This prospective observational study included assessment of therapeutic efficacy of fresh frozen plasma in 100 cirrhotic patients with low prothrombin index. We transfused 20ml/kg body weight of FFP for 40%, 10ml/kg body weight of FFP for 40% and 15ml/kg body weight of FFP for 20% of cirrhotic patients with low PTI with bleeding manifestations. Dose of FFP was decided after considering Body weight, level of PTI, Bleeding manifestations & other comorbidities. Prothrombin index and international normalized ratio in cirrhotic patients were recorded before and after transfusion of fresh frozen plasma, prothrombin index test was done by manual method. Clinical efficacy of fresh frozen plasma transfusion on clinical symptoms like hematemesis, melaena, ecchymosis and petechiae in liver cirrhosis patients was recorded and compared before and after transfusion of FFP. Results: 87% were males and 13% were females and Alcohol was the most common etiological agent in cirrhotic patients. Melaena was seen in 72% of patients, hematemesis in 19% of patients, ecchymosis and petechiae in 20 and 21% of patients respectively. We observed that 20ml/kg body weight dose of FFP transfusion was able to not only improve the PTI in a statistically significant manner, but was also able to improve the INR in statistically significant manner($P<0.05$), showed greater percentage of improvement in clinical symptoms and lastly was found to be more effective for treating the bleeding manifestation with low PTI level and high INR. **Conclusion:** Commonly recommended dose of FFP (10-15 ml/kg body weight) in clinical practice infrequently correct the coagulopathy, so higher dose (≥20ml/kg body weight) may be more effective in correction of coagulopathy.
**Key words:** Fresh frozen plasma, liver cirrhosis, prothrombin time, INR.

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**INTRODUCTION**:
Cirrhosis of liver is a growing cause of significant morbidity and mortality of modernization. Cirrhosis patients have a disturbed balance between procoagulant and anti-coagulant factors and a very poor reserve of these factors leads to increased bleeding risk as well as increased thrombotic risk.This coagulation imbalance is not reflected by conventional coagulation test. Although variceal bleeding remains being the most prevalent

coagulopathy associated exacerbation, thrombotic complications are not un-common in the cirrhotic patients.[1-4] To tackle the bleeding tendencies in cirrhotic patients we can use fresh frozen plasma, vitamin K & other plasma products.for correction of coagulation factors fresh frozen plasma commonly used. Fresh frozen plasma (FFP) is the fluid portion of a fresh unit of whole blood from which erythrocytes, leukocytes and platelets have been removed.It is frozen in a designated time frame usually within 8 hours. It contains all coagulation factors, fibrinogen (400 to 900 mg/unit), albumin, protein C, protein S, antithrombin and tissue factor pathway inhibitor. FFP corrects coagulopathy by replacing or supplying plasma proteins in patients who are deficient in or have defective plasma proteins. Common recommended dose used in clinical practice is 10-15ml/kg body weight but studies shows that this dose is ineffective in correction of coagulopathy in liver cirrhosis so larger doses ≥ 20ml/kg body weight may be required to correct the coagulopathy in cirrhosis.[5]

While the use of fresh frozen plasma is increasing globally, it must be remembered that it is associated with potential risk to the recipient. Many studies have shown a high incidence of inappropriate use of FFP.[5-11] Inappropriate use not only leads to a wastage of limited resources depriving more needy patients, but also leads to an increased healthcare cost and increased risk of transfusion related complications.

Therefore, there is a need for more prudent use of this expensive blood product. Various guidelines for appropriate FFP use have been proposed.[12-17] However many of these are mainly expert consensus rather than recommendations derived from meticulous scientific studies. Moreover, the threshold for PT and aPPT prolongation of >1-1.5 times was based on outdated retrospective studies. PT and aPPT are poor predictors of perioperative bleeding especially in patients with negative bleeding history. Therefore the utility of routine preoperative coagulation testing has been questioned.[18,19]

The prothrombin time (PT) is a test that helps evaluate ability to appropriately form blood clots.PT measures the number of seconds it takes for a clot to form in a sample of blood after substance(reagent) are added. The PT is often performed along with a activated partial thromboplastin time (aPTT) and together they assess the amount and function of proteins called coagulation factors that are an important part of proper blood clot formation. The international normalized ratio(INR) is a calculation based on results of a PT that is used to monitor individuals who are being treated with the blood thinning medication.[4,20-22]

According to British committee for standards in hematology guidelines,[20] bleeding history including family history, details of prior surgeries and anticoagulant treatment should be taken prior to surgery. Patients with negative bleeding history do not require routine preoperative coagulation testing. However, some recent papers still recommend routinely performing PT, aPPT and platelets count prior to surgery and invasive procedure in liver cirrhosis in adults and children.[21] FFP usage has been increasing in our institute since few years.

Hence we took up a study on the institutes of FFP usage with the specific aims of auditing our FFP usage according to the age of patient, indications for FFP administration, appropriate and inappropriate usage of FFP and improvement in PTI/INR with FFP transfusion in liver cirrhosis patients.

**MATERIAL AND METHODS:**

The present prospective observational study was carried out in the Guru Nanak Dev Hospital/ Govt. Medical College, Amritsar. The patients presenting to medical emergency, medical outdoor and indoor with liver cirrhosis on ultrasound abdomen were selected for the purpose.

A total 100 patients with written informed consent were included in the study. Clinical examination and USG abdomen was done in every patient. PTI was done in patients before and after therapy of fresh frozen plasma. The approval of institutional ethics committee of Govt. Medical College, Amritsar was taken before the start of the study.

All liver cirrhotic patients with low PTI with bleeding complications were included in the study. Those patients with other known bleeding disorders were excluded from our study.Patients thus selected was transfused 10-20 ml/kg body weight of fresh frozen plasma (FFP) and therapeutic effect of FFP on the patients was noted. PTI was done at the time of enrolment and after transfusion of FFP.Post transfusion PTI/INR was done within 1 hour of completion of transfusion. All observations were noted on proforma after filling the consent form.

**STATISTICAL ANALYSIS:**

The data was tabulated and analyzed with spss17.0 statistical software. Mean ±SD, p value by chi square test, range and percentages were calculated. One way Anova, Post hoc and student's t test for data and chi square test for consolidation of tables were used. A p value of <0.05 was taken as significant relationship.

**RESULTS**:

In this prospective observational study, out of 100 cirrhotic patients, majority of patients 31% belonged to 41-50 years of age followed by 27% patients between 51-60 years of age. Male population predominated with 87% of males and only 13% of females in our study.

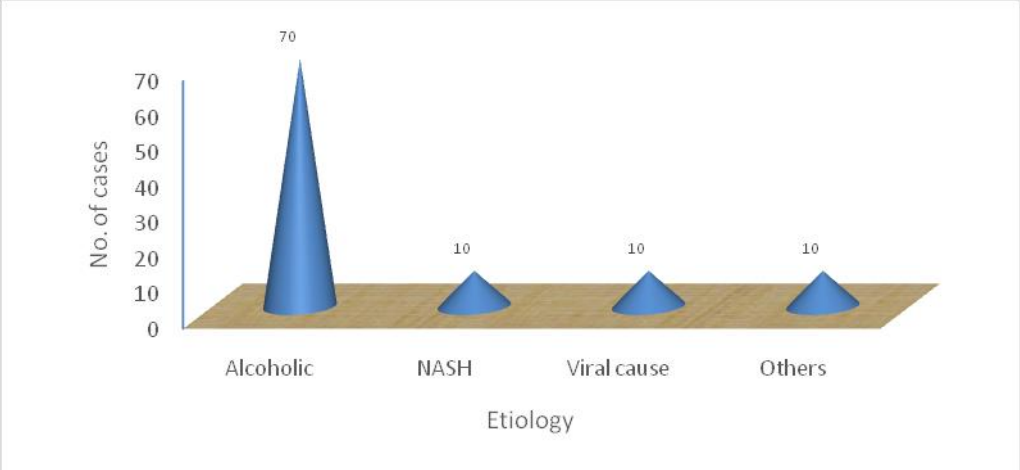
In the present study, 70(70%) cases of cirrhosis were caused by alcohol,10(10%) cases of cirrhosis were non-alcoholic steatohepatitis and 10(10%)cases of cirrhosis were caused by viral hepatitis(Hepatitis C, Hepatitis B) and in remaining 10(10%)cases of cirrhosis. Other etiological factors were found

(cardiac cirrhosis, suspected primary biliary cirrhosis, hemochromatosis and Wilson disease. (TABLE & FIGURE 1)

TABLE 1: DISTRIBUTION OF SUBJECTS ACCORDING TO ETIOLOGY

| Cause | No. of cases | %age |
|---|---|---|
| Alcoholic | 70 | 70 |
| NASH | 10 | 10 |
| Viral cause | 10 | 10 |
| Others | 10 | 10 |
| Total | 100 | 100.0 |

FIGURE 1: DISTRIBUTION OF SUBJECTS ACCORDING TO ETIOLOGY




Our findings showed that majority of cirrhotic patients had weight of 50-74 kg range , while minimum patients 5(5%) were of s body weight was between 75-100 kg. In our study, out of 100 cirrhotic patients, 40(40%) patients received 10ml/kg body weight of FFP, 20(20%) patients received 15ml/kg body weight of FFP, and 40(40%) patients received 20ml/kg body weight of FFP. Dose was decided depending on level of PTI, bleeding manifestations and other comorbidities. When PTI was evaluated in our study, it was observed that 28 patients were having PTI between 80-99%, 54 patients were having PTI between 60-79%, 16 patients were having PTI between 40-59% and 2 patients, PTI was between 20-39%.

Further in our study, We observed a significant rise in PTI and clinical symptoms in patients with FFP transfusion at 20ml/kg body weight (p-value <0.05, average improvement in PTI is 14.11%) and FFP transfusion at 15ml/kg body weight (p-value 0.09, average improvement in PTI is 6.59%) and 10ml/kg body weight (p-value 0.67, average improvement in PTI is1.18%) showed less improvement in PTI and clinical symptoms, which was not statistically significant. So it was concluded that FFP transfusion at 20 ml/kg body weight was more effective in improving the PTI as compared to FFP transfusion at 15ml/kg body weight and 10 ml/kg body weight. 2 patients after transfusion of FFP at 10ml/kg body weight developed mild febrile transfusion reaction.(Figure 2)

While comparing the therapeutic efficacy of FFP transfusion at 10, 15 and 20ml/kg body weight, we observed rise in INR in patients who received FFP at 20ml/kg body weight (p-value 0.01, average improvement in INR was 0.34), which was statistically significant. Although, FFP transfusion at 15ml/kg body weight (p-value 0.19, average improvement in INR was 0.09) and 10ml/kg body weight (P-value 0.74, average improvement was INR is 0.02) showed an improvement, but statistically insignificant. (Figure 3)

Table 2: EFFECT OF FFP ON PTI

| FFP (ml/kg) | Pre-transfusion of FFP, PTI | | Post-transfusion of FFP, PTI | | p-value |
|---|---|---|---|---|---|
| | Mean | SD | Mean | SD | |
| 10 | 72.79 | 12.20 | 73.97 | 13.15 | 0.67 |

| | | | | | |
|---|---|---|---|---|---|
| 15 | 72.60 | 11.64 | 79.19 | 12.59 | 0.09 |
| 20 | 64.79 | 14.04 | 78.90 | 12.97 | 0.01 |
| Total | 69.55 | 13.32 | 76.99 | 13.08 | 0.01 |

Figure 2: EFFECT OF FFP ON PTI

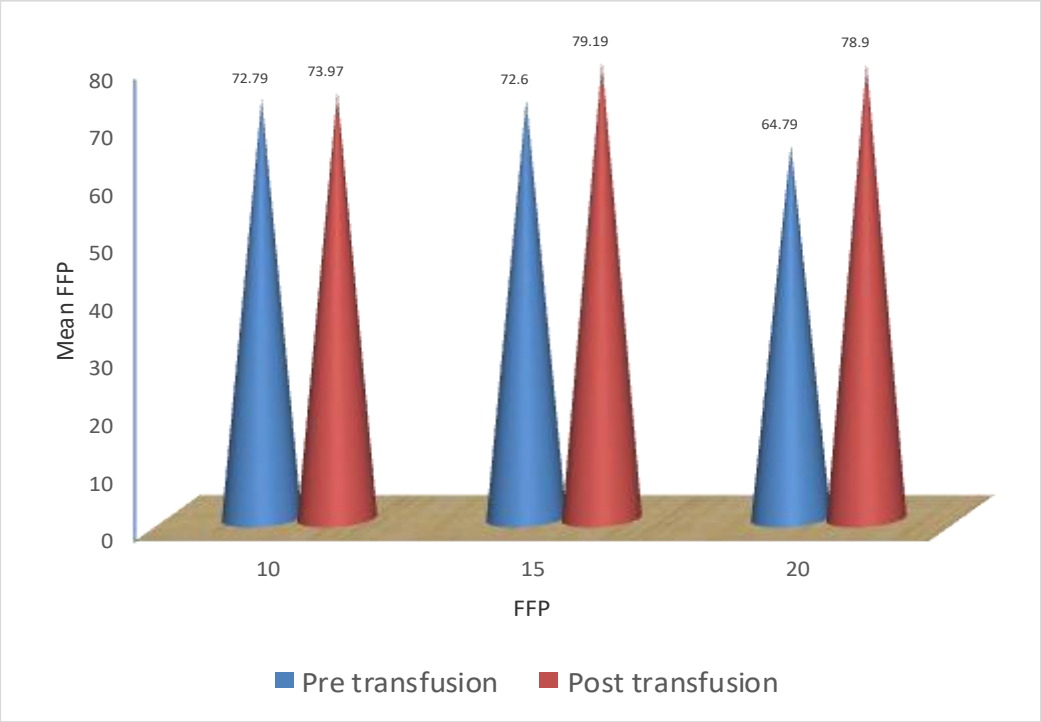
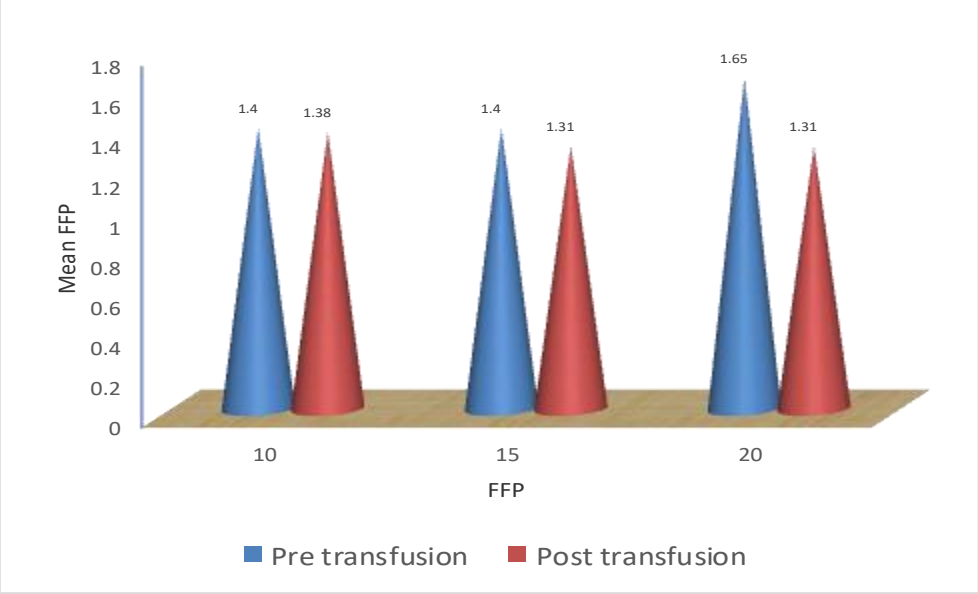



Table 3: EFFECT OF FFP ON INR

| FFP | Pre transfusion of FFP, INR | | Post transfusion of FFP, INR | | p-value |
|---|---|---|---|---|---|
| | Mean | SD | Mean | SD | |
| 10 | 1.40 | 0.26 | 1.38 | 0.28 | 0.74 |
| 15 | 1.40 | 0.24 | 1.31 | 0.221 | 0.19 |
| 20 | 1.65 | 0.62 | 1.31 | 0.37 | 0.01 |
| Total | 1.50 | 0.45 | 1.33 | 0.31 | 0.01 |

Figure 3: EFFECT OF FFP ON INR

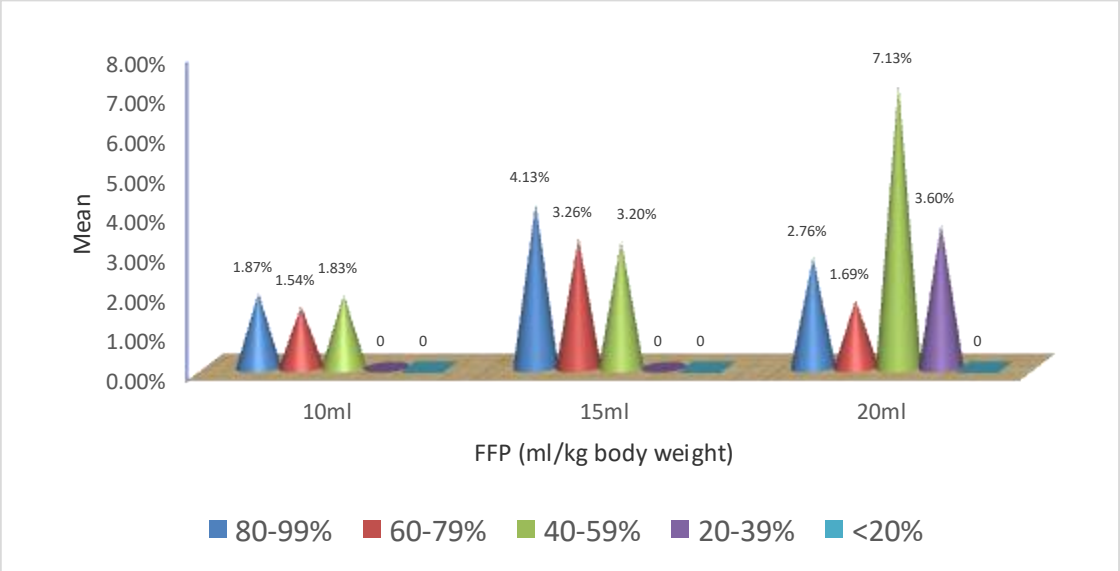


Average improvement in PTI after transfusion of FFP. Cirrhotic patients having PTI between 80-99%. (In this group we decided to transfuse FFP at times despite slightly low PTI as we could not have relieved upon a single test result when patient was having profuse bleeding hence giving patient the benefit of doubt and sometimes transfusion were started before availability of test result in dire emergent situation). 60-79% and 40-59% showed average improvement in PTI of 1.87%, 1.54% and 1.83% after transfusion of FFP at 10ml/kg body weight respectively. After transfusion of FFP at 15ml/kg body weight, patients having PTI between 80-99%, 60-79% and 40-59% showed average improvement in PTI of 4.13%,3.26% and 3.2% respectively. After transfusion of FFP at 20ml/kg body weight, patients having PTI between 80-99%, 60-79%, 40-59% and 20-39% showed average improvement in PTI of 2.76%,1.69%,7.13% and 3.6% respectively. On an average 20ml/kg body weight dose of FFP was able to increase the PTI maximally in all the groups especially in patients who were having lower pretransfusion PTI i.e. especially <60% of PTI.

Table 4: AVERAGE IMPROVEMENT OF PTI AFTER FFP TRANSFUSION

| | **Average Improvement in PTI** | | | | |
|---|---|---|---|---|---|
| PTI groups (FFP (ml/kg body weight) | 80-99% | 60-79% | 40-59% | 20-39% | <20% |
| 10ml | 1.87% | 1.54% | 1.83% | - | - |
| 15ml | 4.13% | 3.26% | 3.20% | - | - |
| 20ml | 2.76% | 1.69% | 7.13% | 3.6% | - |

FIGURE 4: AVERAGE IMPROVEMENT OF PTI AFTER FFP TRANSFUSION




When we evaluated distribution of clinical symptoms after transfusion FFP at 10ml/kg body weight,2 out of 4 patients who had hematemesis,23 out of 26 patients who had melaena,2 out of 3 patients who had petechiae and 3 out of 4 patients who had ecchymosis, showed improvement in symptoms. After transfusion of FFP at 15ml/kg body weight, 11out of 12 patients who had melaena and 6 out of 7 patients who had petechiae and ecchymosis, showed improvement in symptoms. 14 out of 15 patients who had hematemesis and30 out of 34 patients who had melaena and 10 patients who had petechiae and ecchymosis showed improvement in symptoms after transfusion of FFP at 20ml/kg body weight.

TABLE 5: DISTRIBUTION IN CLINICAL SYMPTOMSAFTER TRANSFUSION of FFP

| FFP (ml/kg) | Hematemesis | | Melaena | | Ecchymosis | | Petechiae | |
|---|---|---|---|---|---|---|---|---|
| | Pre transfusion | Post transfusion | Pre Transfusion | Post Transfusion | Pre Transfusion | Post transfusion | Pre Transfusion | Post transfusion |
| 10 | 4 | 2 | 26 | 3 | 3 | 1 | 4 | 1 |
| 15 | - | - | 12 | 1 | 7 | 1 | 7 | 1 |
| 20 | 15 | 1 | 34 | 4 | 10 | 0 | 10 | 0 |

Out of 100 cirrhotic patients with bleeding manifestation,19(19%) patients had hematemesis, in that 16(16%) patients were improved after FFP transfusion,72(72%) patients had melaena in that 64 (64%) patients were improved,20(20%)patients had ecchymosis in that 18 (18%) patients were improved and 21(21%) patients had petechiae in that 19 (19%) were improved after FFP transfusion.

Out of 37 patients who were clinically symptomatic, 30 patients showed improvement in clinical symptoms after transfusion of FFP at 10ml/kg body weight. 23 out of 26 patients who were clinically symptomatic showed improvement in clinical symptoms after transfusion of FFP at 15ml/kg body weight. And 63 out of 69 patients who were clinically symptomatic, showed improvement in clinical symptoms after transfusion of FFP at 20ml/kg bodyweight. These improvement in clinical symptoms were statistically significant (p value <0.05) in all 3 categories of FFP transfusion, but percentage of improvement in clinical symptoms after steatohepatitis and in remaining 10%, cardiac cirrhosis, suspected primary biliary cirrhosis, Wilson's disease and hemochromatosis were the etiological factors. A study by Youssef at el[22]most common etiology being alcohol was seen in 52% of chronic liver disease patients, hepatitis C in 8%, combined in 37% and other etiology in 3% of patients.

To study the efficacy of FFP on PTI, we divided the subjects into 3 groups depending on ml/kg body weight FFP transfused, out of 100 patients 40patients were transfused 10 ml/kg body weight, 20were transfused 15 ml/kg body weight and 40were transfused 20 ml/kg body weight.

Out of 100 cirrhotic patients, 28% of patients were having PTI between 80-99%, 54% of patients were having PTI between 60-79%, 16% of patients were having PTI between 40-59% and in 2% of patients PTI was between 20-39%.

Before transfusion of FFP in 40% of cirrhotic patients, the mean PTI was 72.79±12.20, after transfusion of FFP at 10ml/kg body weight mean PTI improved to 73.97±13.15 (p value is 0.67) which shows little improvement in PTI (average improvement in PTI was1.18%), but which was statistically insignificant. Before transfusion of FFP in 20% of patients with cirrhosis the mean PTI was 72.60±11.64,after transfusion of FFP at 15ml/kg body weight mean PTI improved to 79.19±12.59 (p value is 0.09) which showed improvement in PTI(average improvement in PTI was 6.59%), but which was also statistically insignificant, while in 40% of cirrhotic patients, FFP transfusion at 20 ml/kg body weight, mean PTI of 64.79±14.04, improved to78.9±12.97 (p-value is 0.01) which shows statistically significant improvement in PTI(average improvement in PTI was 14.11%).Our study result is in concordance with the study conducted by the Chowdhury etal.[24] transfusion at 20ml/kg body weight is more as compared to 15ml/kg and 10ml/kg body weight.

**DISCUSSION**:

This is a prospective observational study, in this study we transfused FFP depending on ml/kg body weight in 100 cirrhotic patients with low PTI with bleeding manifestation like hematemesis, melaena, ecchymosis, and petechiae.

Majority of patients 31% belonged to 41-50 years of age followed by 27% patients between 51-60 years of age. Male population predominated with 87% of males and only 13% of females in our study. Similar results were obtained by youssef et al,[22] in which males predominated Mean age was 46.3±10.6 years. In another study by Sukanyaet al[23] 86.3% were males the median age was 47.12±12.36 years.

In our study, we observed that alcohol was the most common etiologic factor, being responsible for occurrence of 70 percent of the cirrhosis cases. In 10% viral cause, and in 10% nonalcoholic Youssef et al[22] also reported similar results which are in concordance our study result i.e. FFP transfusion at 20 ml/kg body weight is more effective than FFP transfusion at 15ml/kg and 10ml/kg body weight.

Therapeutic efficacy of FFP on INR also shows same results, 20ml/kg body weight doseof FFP transfusion was able to improve the INR in a statistically significant manner(P<0.05),(average improvement in INR is 0.34)whereas the 15ml/kg body weight doseof FFP improved INR but the difference was not statistically significant(P>0.05)(average improvement is 0.09),while 10ml/kg body weight dose showed little improvement but statistically insignificant (P>0.05)(average improvement in INR is 0.02),so standard dose of FFP 10-15ml/kg body weight dose was ineffective in statistically improving the INR, so higher doses (≥20ml/kg body weight) of FFP may be required to increase INR in liver cirrhosis. The above our study results were inconcordance with the study by Sukanya B et al[23].

Cirrhotic patients having PTI between 80-99%,60-79% and 40-59% showed average improvement in PTI of 1.87%,1.54% and 1.83% after transfusion of FFP at 10ml/kg body weight respectively. After transfusion of FFP at 15ml/kg body weight, patients having PTI between 80-99%,60-79% and 40-59% showed average improvement in PTI of 4.13%,3.26% and 3.2%respectively. After transfusion of FFP at 20ml/kg body weight, patients having PTI between 80-99%,60-79%,40-59% and 20-39% showed average improvement in PTI of 2.76%,1.69%,7.13% and 3.6% respectively. On an average 20ml/kg body weight dose of FFP was able to increase the PTI. Maximum in all the groups especially in patients who are having lower pretransfusion PTI i,e especially <60% of PTI. This result was in concordance with the study by Youssef at el[22],in retrospective arm(80 patients) after transfusion of 3.75±1.62 units of FFP,

prothrombin time improved from 17.5±4 to 15.9±2, percentage change in PT was 1.5±1.89.and in prospective arm(20 patients),after transfusion of 2.9±1.44 units of FFP, prothrombin time was improved from 20±4.9 to 17.3±2.6.

We also studied the improvement of clinical symptoms like hematemesis, melaena, ecchymosis, petechiae in cirrhosis patients after transfusion of FFP.30 out of37 patients showed improvement in clinical symptoms after transfusion of FFP at 10ml/kg body weight, 23 out of 27 patients showed improvement in clinical symptoms after transfusion of FFP at 15ml/kg body weight, 63 out 69 patients showed improvement in clinical symptoms after transfusion of FFP at 20ml/kg body weight. These improvement in clinical symptoms were statistically significant in all 3 categories of FFP transfusion patients, but percentage of improvement in clinical symptoms after transfusion of FFP at 20ml/kg body weight is more as compared to FFP transfusion at 10ml and 15ml/kg body weight. So higher doses of FFP transfusion at 20ml/kg body weight is more efficacious in correction of coagulopathy this result is in concordance withthe dual study by Youssef et al.[22] Role of fresh frozen plasma infusion in correction of coagulopathy of chronic liver disease suggested fresh frozen plasma infusions using the number of units commonly employed in clinical practice infrequently correct the coagulopathy of patients with chronic liver disease. Higher volumes (6 or more units) may be more effective.

One more study conducted by Baxi et al,[25] a retrospective chart review was used to identify patients with cirrhosis, admitted with upper gastrointestinal bleed.169 patients were included in the study,out of which 111 patients received no FFP,34 received 1-2 units of FFP and 24 received more than 3 units of FFP. Compared to those who received no FFP, patients who received 1-2 units(OR 0.02,p=0.3) or more than 3 units of FFP(0.01,p=0.16) were less likely or no more to have evidence of active bleeding at endoscopy respectively. So higher dose of FFP is required for correction of coagulopathy in liver cirrhosis.

**CONCLUSION**:

This study highlights the facts that alcohol is the most common cause of liver cirrhosis, liver cirrhosis is associated with mild coagulation abnormalities, prothrombin index/ international normalized ratio test can be used as marker for correction of coagulopathy in cirrhosis. Commonly recommended dose of FFP (10-15 ml/kg body weight) in clinical practice infrequently correct the coagulopathy, so higher dose (≥20ml/kg body weight) may be more effective in correction of coagulopathy. Further large scale studies are needed to be conducted to substantiate the findings depicted in our study.

**REFERENCES**:


1. Caldwell SH, Hoffman M, Lisman T, Macik BG, Northup PG, Reddy KR, Tripodi A, et al. Coagulation disorders and hemostasis in liver disease: pathophysiology and critical assessment of current management. Hepatology2006;44:1039-46.
2. Lisman T, Porte RJ. Rebalanced hemostasis in patients with liver disease: evidence and clinical consequences. Blood 2010;116:878-5.
3. Tripodi A, Mannucci PM. The coagulopathy of chronic liver disease. N Engl J Med.2011;365:147-56.
4. Shah NL, Northup PG, Caldwell SH. A clinical survey of bleeding, thrombosis, and blood product use in decompensated cirrhosis patients. Ann Hepatol.2012;11(5):686-90.
5. Chaudhary R, Singh H, Verma A, Ray V. Evaluation of fresh frozen plasma usage at a tertiary care hospital in North India. ANZ Journal of Surgery. 2005;75(7):573-6.
6. Kim CK, Lim JH and Lee WJ. Detection of hepatocellular carcinomas and dysplastic nodules in cirrhotic liver: accuracy of ultrasonography in transplant patients. J Ultrasound Me Prathiba R, Jayaranee S, Ramesh JC, Lopez CG, Vasanthi N. An audit of fresh frozen plasma usage in a tertiary referral centre in a developing country. Malays J Pathol. 2001;23:41–6.
7. Hui CH, Williams I, Davis K. Clinical audit of the use of fresh-frozen plasma and platelets in a tertiary teaching hospital and the impact of a new transfusion request form. Intern Med J. 2005;35:283–8.
8. Kakkar N, Kaur R, Dhanoa J. Improvement in fresh frozen plasma transfusion practice: Results of an outcome audit. Transfus Med. 2004;14:231–5.
9. Soutar RL, Jobanputra S, Tait RC, West of Scotland Consultant Haematologists' Audit Group. A two-phase audit of fresh frozen plasma: A regional approach. Transfus Med. 2004;14:75–6.
10. Luk C, Eckert KM, Barr RM, Chin-Yee IH. Prospective audit of the use of fresh-frozen plasma, based on Canadian Medical Association transfusion guidelines. CMAJ. 2002;166:1539–40d. 2001;20:99–104.
11. Chng WJ, Tan MK, Kuperan P. An audit of fresh frozen plasma usage in an acute general hospital in Singapore. Singapore Med J. 2003;44:574–8.
12. O Shaughnessy DF ,Atterbury C, BoitonMaggsP,et al :Guidelines for the use of fresh frozen plasma ,cryoprecipitate and cryosupernatant.Br J Haematol. 2004;126:11-28
13. Canberra: National Health and Medical Research Council (NHMRC)/Australasian Society of Blood Transfusion (ASBT). Clinical Practice Guidelines. Appropriate Use of Fresh Frozen Plasma and Cryoprecipitate; C. 2001;p.09. Available from: http://www. nhmrc.gov.au
14. Feng CS, Chan YS, Leong S, Au KL, Chu R, Chan J, et al. Guidelines for the appropriate use of fresh frozen plasma. J Hong Kong Med Assoc. 1990;42:106–8.
15. Contreras M, Ala FA, Greaves M, Jones J, Levin M, Machin SJ et al. Guidelines for the use of fresh frozen plasma. British Committee for Standards in Haematology, Working Party of the Blood

Transfusion Task Force. Transfus Med. 1992;2:57–63.
16. Stehling L, Luban NL, Anderson KC, Sayers MH, Long A, Attar S, et al. Guidelines for blood utilization review. Transfusion. 1994;34:438–48.
17. Practice parameter for the use of fresh-frozen plasma, cryoprecipitate, and platelets: Fresh-Frozen Plasma, Cryoprecipitate, and Platelets Administration Practice Guidelines Development Task Force of the College of American Pathologists. JAMA. 1994;271:777–81.
18. Chee YL, Crawford JC, Watson HG, Greaves M. Guidelines on the assessment of bleeding risk prior to surgery or invasive procedures: British Committee for Standards in Haematology. Br J Haematol. 2008;140:496–504.
19. Ewe K. Bleeding after liver biopsy does not correlate with indices of peripheral coagulation. Dig Dis Sci. 1981;26:388–93.
20. Croquet V, Vuillemin E, Ternisien C, Pilette C, Oberti F,Gallois Y et al. Prothrombin index is an indirect marker of severe liver fibrosis. European Journal of Gastroenterology &Hepatology. 2002;14(10):1133-41.
21. Cosmi B, Alatri A, Cattaneo M, Gresele P, Marietta M, Rodeghiero F, et al. Assessment of the risk of bleeding in patients undergoing surgery or invasive procedures: Guidelines of the Italian Society for Haemostasis and Thrombosis (SISET) Thromb Res. 2009;124:e6–12.
22. Youssef WI, Salazar F, Dasarathy S, Beddow T and Mullen KD. Role of fresh frozen plasma infusion in correction of coagulopathy of chronic liver disease: a dual phase study. Am J Gasteroenterol. 2003,98(6):1391-4.
23. Baruah S, Bajpai M. Effect of FFP Transfusion on International Normalized Ratio in Liver Disease Patients. Indian Journal of Hematology and Blood Transfusion. 2018;34(4):719-22.
24. Chowdhury P, Saayman AG, Paulus U, Findlay GP, Collins PW. Efficacy of standard dose and 30 ml/kg fresh frozen plasma in correcting laboratory parameters of haemostasis in critically ill patients. British Journal of Haematology. 2004;125(1):69-73.
25. Baxi AC, Grant S, Teng BJ, Harms MA, Jensen-Otsu E, Strate LL et al. Impact of Fresh Frozen Plasma Transfusion on Upper Gastrointestinal Bleeding in Patients With Cirrhosis: 557. American Journal of Gastroenterology. 2017;112:S296.