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# THE RATE OF INCREASE OF PLATELET COUNT IN THROMBOCYTOPENIA: TRANSFUSIONS VS NON TRANSFUSIONS

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**A R T I C L E I N F O**

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**A B S T R A C T**

***Aim & objectives:*** The aim of the study is to show the effectiveness of diverse treatments in thrombocytopenia. The main objective of the study is to show the effectiveness of various treatment options in Thrombocytopenia patients and to relate the platelet count increment in transfusions and non-transfusions.

***Methods:*** A prospective observational study was conducted on effectiveness of diverse treatments in thrombocytopenia patients from august 2018-january 2019 at regional VR Multi speciality hospital Kurnool.

***Results:*** A total of 51 patients were grouped and categorised into two groups out of them 29.42% of patients undergone platelet transfusion and remaining 70.58% under pharmacological therapy. We recruited the patients based inclusion and exclusion criteria. The patients with platelet count <20,000 per micro Liter will be having high bleeding, so platelet transfusion in those patients was recommended. In our study we were taken only patients who are transfused with single donor. The patients under pharmacological treatment prescribed with different drugs, 16 patients were given with only Carica papaya, 8 treated with Carica papaya & hydrocortisone and 12 were treated with all three drugs starting with Eltrombopag (TRA's).

***Conclusion:*** We concluded that effectiveness of diverse treatments were observed by increments in platelet count in thrombocytopenia. Among these, Transfusions show 71% efficacy. In non transfusions, medications such as Carica papaya showed 21% efficacy, Eltrombopag showed 18.66% efficacy and hydrocortisone showed 0.3% efficacy.



## INTRODUCTION

Thrombocytopenia (THROM-bo-si-to-PE-ne-ah) is a condition in which your blood has a lower than normal number of blood cell fragments called platelets (PLATE-lets).

Platelets are made in your bone marrow along with other kinds of blood cells. They travel through your blood vessels and stick together (clot) to stop any bleeding that may happen if a blood vessel is damaged. Platelets are also called Thrombocytes because a clot also is called a thrombus.[1]

Thrombocytopenia is defined as a platelet count below the lower limit of normal (i.e., <150,000/microliter [150 x $10^9$/L]). Degrees of thrombocytopenia can be further subdivided into mild (platelet count 100,000 to 150,000/microliter), moderate (50,000 to 99,000/ microliter), and severe (<50,000/microliter)[2]. In current study, recruited Thrombocytopenia patients are suffering from dengue fever, hepatitis and patients undergone surgery are also considered.

The management of thrombocytopenia has different treatment options as follow:

- **Blood or platelet transfusions.** If your platelet level becomes too low, your doctor can replace lost blood with transfusions of packed red blood cells or platelets.
- **Medications.** If your condition is related to an immune system problem, your doctor may prescribe drugs to boost your platelet count. The first-choice

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drug may be a corticosteroid. If that doesn't work, he or she may try stronger medications to suppress your immune system.

- **Surgery.** If other treatment options don't help, your doctor may recommend surgery to remove your spleen (Spleenectomy)[3].

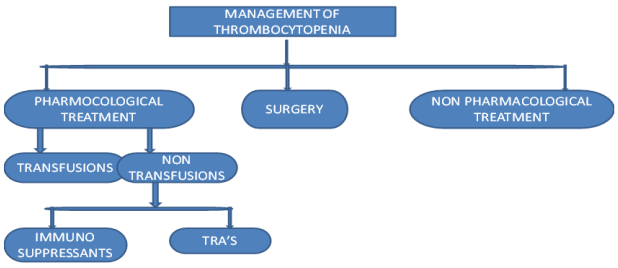



**Fig 1**

In our study therapy starting with Carica papaya and hydrocortisone for mild thrombocytopenia patients, moderate thrombocytopenia was treated with Thrombopoetin receptor agonists (TRA's) and Platelet transfusion was recommended for patients with severe thrombocytopenia.

Eltrambopag was the preferred TRA in current study with dose of 50 mg once daily by oral route. Hydrocortisone was the preferred corticosteroid and Random donor platelet transfusion was done in patients with severe Thrombocytopenia.

## RESEARCH METHODOLOGY

**Study Design:** Prospective observational study.
**Study Site / Place:** VR multi speciality hospital, Kurnool
**Study Period:** 6 months (August – January)
**Study Population:** 51 patients
**Patient Enrollment:** Patients were enrolled in the study based on inclusion and exclusion criteria.

***Inclusion criteria***

- Patients with Thrombocytopenia
- Patients who are under the therapy with antibiotics and blood platelet transfusion.
- Ages to be considered >10 years.
- Either gender is considered.
- Collected Thrombocytopenia cases randomly

***Exclusion criteria***

- Patients with history of platelet transfusion and severe bleeding(WHO grade 3 and 4)
- Patients with age <10 years.
- Patients who were unconscious.
- Patients with Pseudo thrombocytopenia.

***Study Materials:*** a specially designed

Annexure-I [Patient standard data collection form(I.P)]

***Study procedure***

- Patients were recruited based on prospective observational study from VR multi speciality hospital, Kurnool.
- The patients were categorized male and female. Further the patients are classified according to their age group. Then patients were categorized according to their gender.
- We have collected the cases irrespective of disease where thrombocytopenia is a condition
- Then the patients were classified according to transfusions and pharmacological therapy
- Various treatments are given in the patients which include carica papaya, corticosteroids and TRA's.
- Platelet transfusions were given when the platelet count was below 40,000cells/cumm and in conditions like abdominal cramps and bleeding.
- We had calculated the percentage of platelet increment by using the formula:
- (Final day platelet count – initial platelet count / final day platelet count) x100.

***Statistical Analysis***

The collected data was analysed and the information was tabulated as per study objective using Microsoft excel.

## RESULTS

In our study we screened 51 thrombocytopenia patients. Out of 51 patients 30(58%) were male and 21(42%) were female.

Among 51, fifteen patients were undergone platelet transfusion and 36 patients under pharmacological therapy (non- transfusions).

***Types of Therapy***

In our study the Thrombocytopenic patients are differentiated into 2 groups, the first group receiving pharmacological therapy and the other group underwent Platelet Transfusion.

***Pharmacological group (non transfusion group) -*** In our study we screened total 36 cases under non transfusions. Out of 36 patients, 23 were male and 13 were female.

Out of 36 patients, 12(33.3%) were found between the age group of 11-20, 9(25%) were in between 21-30, 6(16.6%) were in between 31-40, 2(5.5%) were in between 41-50, 4(11.1%) were in between 51-60, 1(2.7%) were in between 61-70, 1(2.7%) were in between 71-80, 1(2.7%) were in between 81-90.

Different classes of drugs given in thrombocytopenic patients, the first preferred was treating with carica leaf extract (carica papaya), later with hydrocortisone and Thromboietin receptor agonists (Eltombopag) was preferred to patients having very low platelet count.

In our study 36 patients were under pharmacological treatment with different drugs among them 16 patients were given with only Carica papaya, 8 patients were treated with Carica papaya + hydrocortisone, and 12 were treated with all the three drugs starting with Carica papaya, hydrocortisone and Eltrombopag (TRA).

Following pie chart indicates the patients under treatment with different classes of drugs:

**Patients under pharmacological treatment**

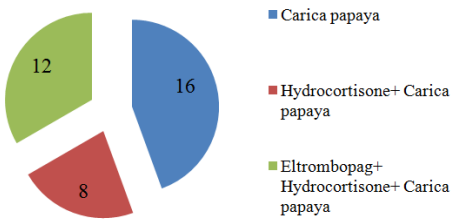



**Fig 2**

***Patients with Carica papaya***

The following table indicates the amount of platelet count increment and the percentage of increased platelet count for four days in patients who were under treatment with Carica papaya. Among 16 patients, the platelet count increment was seen in 14 patients, but in two patients platelet count was not improved.

The amount of platelet count improvement was obtained by taking difference between final day platelet count i.e., Day- 4 and initial platelet count. The percentage of increased platelet count was calculated by following formula:

= (Final day platelet count – initial platelet count / final day platelet count)*100

***Patients with Carica papaya + Hydrocortisone***

The following table shows the percentage of increased platelet count of patients who were under treatment with Carica papaya + hydrocortisone. Among 8 patients, the platelet count was improved but in 2 patients, platelet count said to be declined.

***Patients with Eltrombopag***

The patients who were not responding to Carica papaya and Hydrocortisone treatment, they were given along with Thrombopoietin receptor agonist, eg: Eltrombopag. The combination of immunosupressants with Thrombopoietin receptor agonists given to the 12 patients, among them most of the patients platelet count was improved, but few of them where shown non respond to the treatment when it was taken for 4 days. The following table shows the percentage of increased platelet count for four days.

***Transfusion group***

The patients who are disease severity found to be having very low platelet count and also not responding to the pharmacological treatment, should be treated by transferring of platelets.

**Table 1**

| Patients with Carica papaya | | | | | | | |
|---|---|---|---|---|---|---|---|
| **S. no** | **Initial platelet count** | **Day-1** | **Day-2** | **Day-3** | **Day-4** | **Amount of platelet count improvement** | **Percentage of increased platelet count** |
| 1 | 1,11,000 | 1,25,000 | 88,000 | 92,000 | 1,01,000 | -10,000 | -9% |
| 2 | 82,000 | 65,000 | 59,000 | 86,000 | 1,07,000 | 25,000 | 23.36% |
| 3 | 72,000 | 45,000 | 30,000 | 65,000 | 85,000 | 13,000 | 15.29% |
| 4 | 1,35,000 | 1,23,000 | 1,26,000 | 1,75,000 | 2,07,000 | 72,000 | 34.78% |
| 5 | 92,000 | 90,000 | 1,21,000 | 1,40,000 | | 48,000 | 34.28% |
| 6 | 75,000 | 77,000 | 92,000 | 1,21,000 | | 46,000 | 38.01% |
| 7 | 1,10,000 | 1,48,000 | 1,51,000 | | | 41,000 | 27.15% |
| 8 | 75,000 | 89,000 | 1,01,000 | | | 26,000 | 25.74% |
| 9 | 94,000 | 69,000 | 82,000 | 99,000 | 1,30,000 | 36,000 | 27.69% |
| 10 | 1,31,000 | 90,000 | 1,43,000 | | | 12,000 | 8.39% |
| 11 | 1,33,000 | 1,24,000 | 1,23,000 | | | -10,000 | -8.13% |
| 12 | 1,05,000 | 1,06,000 | 1,25,000 | 1,35,000 | | 30,000 | 22.22% |
| 13 | 1,34,000 | 1,53,000 | | | | 19,000 | 12.41% |
| 14 | 1,22,000 | 1,19,000 | 1,45,000 | | | 23,000 | 15.86% |
| 15 | 1,37,000 | 1,45,000 | 1,53,000 | | | 16,000 | 10.45% |
| 16 | 80,000 | 89,000 | 83,000 | 92,000 | 1,45,000 | 65,000 | 44.82% |
| | | | Average | | | 28,250 | 21% |

**Table 2**

| Patients With Carica + Hydrocortisone | | | | | | | |
|---|---|---|---|---|---|---|---|
| **SNo** | **Initial platelet count** | **Day-1** | **Day-2** | **Day-3** | **Day-4** | **Amount of platelet count improvement** | **Percentage of increased platelet count** |
| 1 | 1,30,000 | 1,07,000 | | | | -23,000 | -21.49% |
| 2 | 1,13,000 | 77,000 | 83,000 | 1,16,000 | 1,23,000 | 10,000 | 8.13% |
| 3 | 98000 | 76,000 | 82,000 | 1,03,000 | | 5,000 | 4.85% |
| 4 | 1,86,000 | 1,44,000 | 81,000 | 1,34,000 | | -52,000 | -38.80% |
| 5 | 1,36,000 | 1,31,000 | 1,37,000 | | | 1,000 | 0.72% |
| 6 | 1,42,000 | 1,32,000 | 1,58,000 | 1,56,000 | | 14,000 | 8.97% |
| 7 | 67,000 | 72000 | 79000 | 85000 | | 18,000 | 21.17% |
| 8 | 1,38,000 | 1,70,000 | | | | 32,000 | 18.82% |
| | | | Average | | | 625 | 0.30% |

The patients with platelet count <20,000/ microL will be having high risk of bleeding, the platelet transfusion in those patients was recommended. The prophylactic platelet transfusion was not recommended in low risk patients. The patients with low platelet count (<10,000/ microL) having high risk of bleeding and patients with platelet count <20,000/microL having moderate risk of bleeding were recommended for therapeutic platelet transfusion.

The platelet transfusions are mainly 2 types Single Donor Platelet transfusion and Random Donor Platelet transfusion. In our study we are taken only patients who are transfused with Single Donor.

Out of 51 patients 15 patients were found to be transfused with Single donor platelet transfusion. Out of 15 patients 7 are male and 8 are female.

count increment for four days of patients who were undergone platelet transfusion was shown in following table. The percentage of increased platelet count was calculated.

The above table shows the amount of platelet increment and percentage of increased platelet count. The platelet increment was found to be increased in all patients when it was calculated for four days. The post transfusion platelet increment for 24 hrs was found to be 25,000 to 40,000/ microL.

The following graph shows the percentage of platelet count increment in various treatments of Thrombocytopenia patients.

**Table 3**

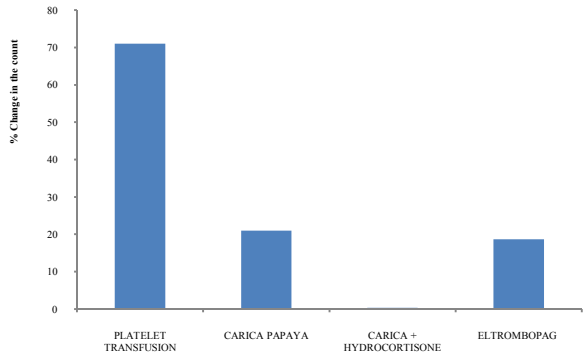
| ELTROMBOPAG | | | | | | | |
|---|---|---|---|---|---|---|---|
| **S.NO** | **Initial platelet count** | **DAY-1** | **DAY-2** | **DAY-3** | **DAY-4** | **Amount of platelet count improvement** | **Percentage of increased platelet count** |
| 1 | 85,000 | 69,000 | 58,000 | 77,000 | 98000 | 13,000 | 13.26% |
| 2 | 93,000 | 71,000 | 61,000 | 75000 | 88000 | -5,000 | -5.68% |
| 3 | 48,000 | 36,000 | 32,000 | 34,000 | 62,000 | 14,000 | 22.58% |
| 4 | 1,29,000 | 82,000 | 51,000 | 92,000 | 1,35,000 | 6,000 | 4.44% |
| 5 | 66,000 | 54,000 | 52,000 | 70,000 | 99,000 | 33,000 | 9.09% |
| 6 | 62,000 | 26,000 | 24,000 | 54,000 | 92,000 | 30,000 | 32.60% |
| 7 | 35,000 | 38,000 | 62,000 | 87,000 | | 52,000 | 59.77% |
| 8 | 69,000 | 37,000 | 42,000 | 54,000 | 79,000 | 10,000 | 12.65% |
| 9 | 48,000 | 25,000 | 30,000 | 29,000 | 49,000 | 1,000 | 2.04% |
| 10 | 98,000 | 92,000 | 49,000 | 65000 | 89,000 | -9,000 | -10.11% |
| 11 | 56,000 | 43,000 | 1,15,000 | | | 59,000 | 51.30% |
| 12 | 51,000 | 31,000 | 55,000 | 75,000 | | 24,000 | 32% |
| | | | Average | | | 19,000 | 18.66% |

**Table 4**

| S. No | Initial count | After transfusions | | | | Amount of platelet count improvement | Percentage of increased platelet count |
|---|---|---|---|---|---|---|---|
| | | Day 1 | Day 2 | Day 3 | Day 4 | | |
| 1 | 18,000 | 35,000 | 83000 | 1,01,000 | 1,12,000 | 94,000 | 83.92% |
| 2 | 17,000 | 20,000 | 22,000 | 72,000 | | 55,000 | 76.38% |
| 3 | 24,000 | 38,000 | 42,000 | 79,000 | | 55,000 | 69.62% |
| 4 | 11,000 | 21,000 | 34,000 | 56,000 | | 45,000 | 80.35% |
| 5 | 24,000 | 93,000 | 1,39,000 | 2,65,000 | 3,68,000 | 3,44,000 | 93.47% |
| 6 | 25,000 | 45,000 | 34,000 | 21,000 | 41,000 | 16,000 | 39.02% |
| 7 | 18,000 | 37,000 | 32,000 | 36,000 | 41,000 | 23,000 | 56.09% |
| 8 | 25,000 | 32,000 | 45,000 | | | 20,000 | 44.44% |
| 9 | 12,000 | 35,000 | 70,000 | 96,000 | | 84,000 | 87.5% |
| 10 | 39,000 | 56,000 | 51,000 | 52,000 | 57,000 | 18,000 | 31.57% |
| 11 | 13,000 | 55,000 | 90,000 | | | 77,000 | 85.55% |
| 12 | 30,000 | 18,000 | 33,000 | 52,000 | 90,000 | 60,000 | 66.66% |
| 13 | 23,000 | 40,000 | 62,000 | 90,000 | 1,35,000 | 1,12,000 | 82.96% |
| 14 | 28,000 | 55,000 | 73,000 | 1,00,000 | 1,50,000 | 1,22,000 | 81.33% |
| 15 | 25,000 | 55,000 | 64,000 | 88,000 | 1,25,000 | 1,00,000 | 80% |
| | | | **Average** | | | **49,727** | **71%** |

Out of 15 patients, 5(33.3%) patients were found between the age group 11-25, 4 (26.6%) were in between 26-40, 5(33.3%) were in between 41-65, 1 (6.6%) was in between 66-80.

The patients who are with platelets less than 40,000/ microL had gone SDP transfusion. The amount of platelet




***Percentage change in the count***

## DISCUSSION

Thrombocytopenia is defined as a platelet count below the lower limit of normal (i.e., <150,000/microliter [150 x $10^9$/L]). Degrees of thrombocytopenia can be further subdivided into mild (platelet count 100,000 to 150,000/microliter), moderate (50,000 to 99,000/ microliter), and severe (<50,000/microliter)

- Platelet transfusion is indicated for the treatment and prevention of bleeding in patients with
- severe thrombocytopenia and/or impaired platelet production and/or function.
- Platelet transfusion is indicated for all patients with clinically significant bleeding in whom thrombocytopenia is thought to be a major contributory factor.
- Prophylactic platelet transfusion may be indicated in certain clinical scenarios.
- Each platelet transfusion should be an independent clinical decision and take into account the relative risks and benefits to the patient.
- Platelet transfusions are not indicated in all causes of thrombocytopenia, and may be contraindicated in certain conditions.

Eltrombopag (el trom' boe pag) is a small molecular weight peptide-like molecule that binds to the transmembrane domain of the thrombopoietin receptor and causes its activation and the proliferation and differentiation of megakaryocytes, with a resultant increase in synthesis and release of platelets[4].
We had calculated the percentage of platelet increment by using the formula

(Final day platelet count – initial platelet count / final day platelet count)*100.

In our study, for mild thrombocytopenia patients carica and hydrocortisone were preferred and in moderate thrombocytopenia patients eltrombopag was preferred.

In a study conducted by Kulkarni N, 64 dengue patients with platelet count less than 20,000/µL received multiple units of random donor platelets. They showed an increment of > 50,000/µL. This study was similar to our study, where we have collected 51 Thrombocytopenia patients among them 15 patients had received Single Donor platelet transfusion. In that 15 patients most of them shown platelet increment of > 45,000µL.

A study on Unfurling the Rationale use of Platelet Transfusion conducted by Pallavi *et al*. According to their study patients who have platelet count less than 40,000µL are recommended for platelet transfusion. They have categorized the patients based on risk of bleeding, High risk, moderate, low and no risk groups based on their platelet count of <20,000, 21-40,000, 41-100,000, and > 100,000/cumm, respectively at the time of admission.[5] This study was supportive to our study, where in our study, we recruited 51 Thrombocytopenia patients among them 15 patients undergone platelet transfusion who had platelet count <40,000µL,it was appropriate platelet transfusion according to the above study. 6 out of 15 patients had platelet count <20,000µL who were at high risk, remaining 9 patients had platelet count 21- 41,000µL who were at moderate risk. The remaining 36 patients had platelet count of >40,000µL, undergone treatment with different classes of drugs. Majority of them shown platelet increment when treated with Carica papaya extract and the patients who supposed to be non responders to the Carica was treated with Immunosuppressants. TRA's are the option for the patients whose platelet count was not improved by Immunosuppressants, and platelet count less than 70,000µL. In our study 12 of 36 non transfused patients treated with Eltrombopag (TRA).

K.C. Shashidhara conducted a study in JSS medical college, Mysore, Karnataka. On Effect of High Dose of Steroid on Platelet count in Acute Stage of Dengue Fever with Thrombocytopenia, they concluded that high dose of steroids was ineffective in increasing of platelets in Dengue fever[6]. Our study was supported by this study, as in our study hydrocortisone was given as treatment in some patients which found to be nil increment of platelets. As above study states that in dengue fever role of steroids is ineffective in platelet increase, in present study most of the cases are dengue fever the percentage of platelet increment was found to be 0.3%.

P. Pallavi *et al*., conducted a study on unfurling the rationale use of platelet transfusion in dengue fever in JSS university hospital for a period of 8 months. [5] Chuansumrit *et al*., study showed that high percentage of dengue cases in age group of 10-14 years, while ayyub *et al*., lye *et al*., noted adult preponderance in age group of 20-40 years. Our study showed that there is a high risk of thrombocytopenia in age group of 11-25 years & 41-55 years in platelet transfused patients. In non-transfused patients there is a high risk of developing thrombocytopenia in age group of 11-20 years.

Kumar *et al*., also observed that the demands for platelet transfusion were mostly received as a panic reaction during the epidemic of dengue fever. Observing a falling platelet count if the count were above $20_x10^9$/l [7]. In our study platelet transfusion was done when platelet counts falls below 9,000 cells/cumm without any specific indications.

Amoolya bhat *et al*., conducted a study on effectiveness of pooled platelet transfusion in concordant nad discordant groups among dengue patients, showed that there is no role for prophylactic platelet transfusion therapy in dengue patients, many clinicians transfuse platelets to correct thrombocytopenia during the critical phase of recovery

from dengue infections to avoid hemorrhagic complications. [8] In our study, we observed that no patient received prophylactic platelet transfusion in thrombocytopenia condition, until the patient's platelet count was less than 20,000cells/cumm, and with complications like bleeding & abdominal cramps.

## CONCLUSION

In this study, 51 patients were collected- among this 15(29.42%) patients were transfused & remaining 36(70.58%) patients were treated with medications.

We have concluded that effectiveness of diverse treatments were observed by increments in platelet count. in thrombocytopenia. Those include Carica papaya, Hydrocortisone, Eltrombopag & transfusions. Among these, transfusions were shown more effective, where Carica and Eltrombopag were shown moderate efficacy and hydrocortisone was seem to be less effective.

Among these transfusions showed 71% efficacy. In non-transfusions, medications such as Carica papaya showed 21% efficacy, Eltrombopag showed 18.66% efficacy and Hydrocortisone showed 0.3% efficacy.

In this study, the sample size was too small and unequal distribution of patients were seen in transfusions and non-transfusions to compare the data. We didn't observe any complications and risk factors during the collection of data. The role of pharmacist in our study is to improve the patient compliance and quality of life.

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