

Role of Fresh Frozen Plasma(FFP) and Single Donor Platelets(SDP) in Treatment of Dengue and Dengue like illness

Seshagiri G¹, Mahesh Reddy J², Samar Rania Mazhar³, Abhignya CH⁴, Ram Narasimha Reddy V⁵

¹ Associate Professor

² Assistant Professor

³ Post graduate

⁵ Professor and HOD

Department of Paediatrics
Chalmeda Anand Rao
Institute of Medical Sciences
Karimnagar-505001
Telangana, India.

⁴ Senior Resident
Department of Paediatrics
Nilofer Hospital
Hyderabad, Telangana.

CORRESPONDENCE:

Dr. Mahesh Reddy J
MD(Paediatrics)
Assistant Professor
Department of Paediatrics
Chalmeda Anand Rao
Institute of Medical Sciences
Karimnagar-505001
Telangana, India.
E-Mail: Maheshjillela@gmail.com

ABSTRACT

Background: Dengue is the most common mosquito borne, epidemic arboviral infection. The case fatality rate is 20% but with timely intervention can be reduced <1%, bleeding and shock are its dreaded complication. In this study transfusion of blood is not taken into consideration as it may lead to adverse effects like volume overload hence this study is on efficacy and outcome after transfusion of fresh frozen plasma and single donor platelets in cases of dengue and dengue like illness.

Materials and Methods: The study design was a prospective and analytical observational study over a sample size of 200 patients who were diagnosed with dengue or dengue like illness with platelet count of less than 30000 requiring FFP and SDP transfusion were recruited.

Results: 100 patients out of 200 were given FFP transfusion alone with increase in mean platelet with p value of <0.001 which is highly significant and in this study 26 patients out of 200 were given SDP transfusion alone the mean increase in platelets with p value of 0.023. And 74 patients out of 200 were given FFP followed by SDP with mean increase of platelets with a p value of <0.001. The mean duration of hospital stay with FFP followed by SDP has significant p value

Conclusion: A rise in platelets with significant p value was found in patients given FFP alone, SDP alone and in FFP followed by SDP. The mean duration of hospital depends on platelet count and number of transfusions given accordingly. Hence significant p value was found to be seen in FFP followed by SDP where there was not only increase in platelets but also effective in hospital stay wise.

Keywords: Thrombocytopenia, bleeding, fresh frozen plasma, single donor platelet

INTRODUCTION

Dengue is arboviral mosquito borne infection, an estimated 500,000 people with severe dengue infection require hospitalization annually and 90% of them are children. Without proper treatment, the case fatality rate in severe dengue is more than 20% and with timely intervention, it can be reduced to <1%.^[1,2]

Bleeding and shock are the most dreaded complications in children with dengue fever leading to high mortality.^[3]

The dengue virus is an RNA virus of family Flaviviridae with four major serotypes. Once inside the circulation it

binds to Langerhans cells and enters them through binding between viral proteins and membrane on the Langerhan cells. The dengue virus has 3 structural proteins namely capsid(C), precursor membrane (prM) and envelope protein (E) and 7 nonstructural proteins namely NS1, NS2, NS2B, NS3, NS4A, NS4B and NS5.

The NS1 antigen is highly conserved glycoprotein and secreted during initial phase of illness. It disappears as antibodies appear and declines as illness advances. The specificity is 100% and sensitivity in first 4 days is 90% in primary dengue.

Following dengue infection 80% of patients show

detectable IgM antibodies by day 5, 99% by day 10 and peaks by day 14. [4]

Dengue leads to endothelial damage and capillary leak causing 3rd space losses and further leads to vascular insufficiency and hypovolemic shock. This further leads to hemoconcentration with increasing packed cell volume. [5]

Judicious fluid therapy remains the key of treatment. [6] The complications like haemorrhagic manifestations, coagulopathy has warranted the use of blood transfusion along with platelets, fresh frozen plasma and cryoprecipitate. [7]

Since blood transfusions involves risks and associated with complications, here we emphasize on efficacy and outcome of fresh frozen plasma and single donor platelets in dengue and dengue like illness.

MATERIALS AND METHODS

Study Design

It is a prospective and analytical observational study over a sample size of 200 patients who were diagnosed with dengue or dengue like illness with platelet count of less than 30000 requiring FFP and SDP transfusion.

Sample Size:

Total of 200 of patients were included in this study.

Study Centre:

Inpatient Admissions in PICU Department of Paediatrics, Chalmeda Anand Rao Institute of Medical Sciences

Study Duration:

The duration of study is from August 2019-January 2020

Inclusion Criteria

- Serologically confirmed cases of dengue with platelet counts < 30,000cells/cu mm
- Cases of dengue like illness with counts < 30,000 cells/cu mm.
- Children between the age of 0 to 14 year

Exclusion Criteria

- Serologically confirmed cases of dengue and cases of dengue like illness with counts > 30,000 cells/cu mm with no warning signs.
- Other cases of thrombocytopenia (infective conditions like malaria, Rickettsial fever, Enteric fever others like ITP and other platelet disorders)
- Patients refusing transfusion.
- Patients refusing to give consent

RESULTS

Table 1: Age wise NS1Ag and IgM Distribution

	Total	Positive	Negative	Chi Square	P Value
NS1	200	109	91	4.677	0.186
IgM	200	97	102	2.218	0.62

The following table shows the no of cases with positive NS1 Antigen and IgM with a pvalue of 0.186 and 0.62 respectively which is not significant.

Table 2: Platelet count in NS1Ag

NS1Ag	No.	Mean	p-value
Positive	109	18990.83	0.02
Negative	91	21131.81	
Total	200	19965	

Table 3: This table shows Platelet count with FFP and SDP

FFP	MEAN	P-VALUE
YES	20678	<0.001
NO	15192.3	
SDP	MEAN	P-VALUE
YES	16910	<0.001
NO	23020	

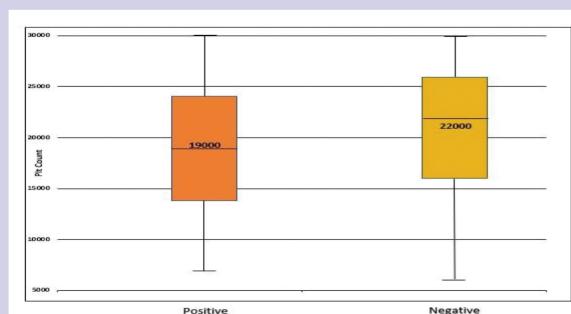
Table 4: Mean values of platelets at 12 and 24 hrs after transfusion with FFP followed by SDP

Platelets	Total no of patients given	Mean	p-value
At 12hrs	74	18918.9	<0.001
At 24hrs	74	43729.7	

Here it shows an increase in the platelet count with FFP followed by SDP with a significant p-value of <0.001 which is highly significant.

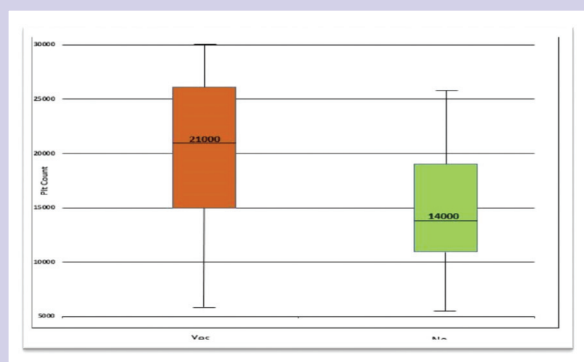
Mean duration of hospital stay in FEP (Table 5) or SDP (Table 6) alone and with FEP followed by SDP

As explained by the above(graph 2 and graph 3) table the counts had a positive outcome by giving FFP or SDP Transfusion alone with a p value <0.001 which is highly significant. Apart from this it was observed that the lesser the platelet the more was the requirement of transfusion, hence platelet count at presentation has significant role in in deciding the no of total transfusion but with a positive outcome. The platelet count observed at 12 and 24hrs post FFP or SDP alone transfusion also had significant p value <0.001.



Graph 1: Shows mean platelet count in cases with NS1Ag which is significant with a p value of 0.02.

As the study is based on transfusion of fresh frozen plasma and single donor platelets separately or together here are the results obtained post transfusion with FFP and SDP alone.



Graph 2: The above graph depicts platelet count in patients transfused with FFP alone.

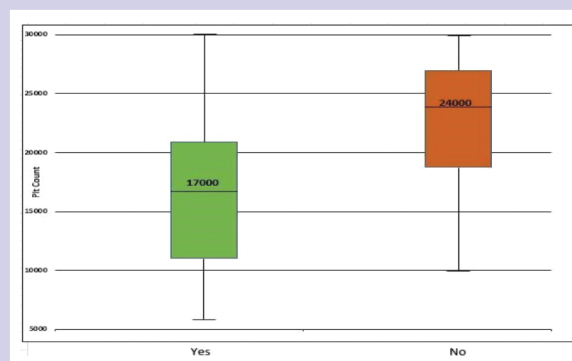
Table 5: This table depicts the effect of FFP alone in average duration of hospital stay

No of FFP	Total no of patients given	Mean	p-value
1	78	5.03	0.766
2	20	5.25	
3	2	5	

As mentioned before the hospital duration depends on the number of transfusions and also on the severity of patient which further contributes to p-value.

DISCUSSION

Patients with acute febrile illnesses in a tropical country like India usually have an infectious etiology and may



Graph 3: The above graph depicts platelet count trend in patients who received SDP.

Table 6: This table shows the effect SDP on average duration of hospital stay No of SDP

No of SDP	Total no of patients given	Mean	p-value
1	25	5.28	0.852
2	1	5	

Table 7: This table depicts the duration of hospital stay in patients with FFP followed by SDP

FFP f/b SDP	Total no of patients given	Mean	p-value
1	52	5.4	<0.001
2	20	7.05	
3	2	10	

have associated thrombocytopenia.^[8] Infections like malaria, dengue, typhoid, and leptospirosis are some common causes of fever with thrombocytopenia the explosive release of pro-inflammatory cytokines in patients with dengue virus infection has cascading effects on endothelial cells lining blood vessels so that the endothelial lining resembles a 'war zone'. Bleeding and shock are the dreadful complications; this sticky endothelium causes platelets to adhere to it thus decreasing number of free floating platelets. The clinical features include febrile illness associated with maculopapular rash and symptoms of myalgia, headache and arthralgia.^[9]

Bleeding is one of the life threatening manifestation due to low platelet count and can manifest as melena, epistaxis, oral and palatal bleed associated with petechial rash. The warning signs in dengue includes abdominal

pain, persistent vomiting, mucosal bleed, respiratory distress and shock due to third space losses.

Children with severe dengue show increasing hematocrit and low platelet count with low leukocyte count with lymphocyte predominance. Serum albumin and total proteins are reduced but more marked in patient with severe dengue.^[10] The virus leads to a cascade of endothelial damage in concert with release of pro-inflammatory cytokines and lead to fluid losses and loss of intravascular volume and leading to further circulatory insufficiency and hypovolemic shock.^[11,12]

Fluid therapy is the cornerstone step in the management of dengue. Stable cases are encouraged to take good amount of oral fluids but complications like increased capillary permeability, thrombocytopenia, coagulopathy and haemorrhagic manifestation, warrant intravenous fluid therapy with ringer lactate or normal saline, packed red cell, platelets and fresh frozen plasma transfusions.^[13,14]

Blood transfusion services constantly face challenges year after year during dengue outbreaks due to lack of evidencebased guidelines for clinical use of blood components.^[15,16] The demand for Platelets and Fresh Frozen Plasma is increasing due to increasing number of cases with severe dengue.

Comparison studies were done and according to R.N Makroo,V Raina most of the patients receiving platelet transfusion recovered completely in 2 to 5 days with increase in counts and hospital varied on severity of infection.^[17]

According to KH Sellaheewa et al in a prospective randomised study on effectiveness of fresh frozen plasma in dengue patients concluded that Fresh Frozen Plasma increases the platelet count in first 12hrs of treatment.^[18]

In our prospective observational study, out of the 200 children enrolled in the study few patients required multiple transfusions based on requirement like expedition in platelet counts, persistent bleeding manifestations, hypotension and signs of capillary leak.

Limitations:

- Viral antibody titres were not done to diagnose primary and secondary dengue precisely. Only qualitative IgM was done quantitative analysis and IgG titre analysis could not be done.
- Serotypes were not done. So, the predominant serotype was not identified.
- Treatment modalities like type of fluid used, need for inotrope support, ventilator support, need for blood products were not studied

- Prevalence and type of bleeding manifestations and the effect of transfusions in their outcome were not assessed.
- In cases where rapid diagnostic test for dengue was negative, we could not assess serological markers for other dengue like illness.

CONCLUSION

In our study with 200 cases of dengue and dengue like illness a rise in platelets was observed in patients receiving FFP alone, SDP alone and in FFP followed SDP. The mean duration of hospital depends on platelet count and no of transfusions given accordingly. Hence, significant p value was found to be seen in FFP followed by SDP where there was not only increase in platelets but also effective in hospital stay wise.

ACKNOWLEDGEMENTS:

Authors would like to thank professor Late Dr.Madoori Srinivas.

CONFLICT OF INTEREST:

The authors declared no conflict of interest.

FUNDING: None

REFERENCES

1. Paul Scott J. Platelet and Blood Vessel Disorders. In: Kingman RM, Stanton BF, St Game III JW Schurz. Nelson Textbook of Paediatrics. 20th edition. Elsevier ; Philadelphia; 2016; 484-2400.
2. WHO. Dengue and Dengue Hemorrhagic fever. Factsheet N 117, revised May2008. Geneva, World Health Organization, 2008.
3. World Health Organization, Regional Office for South-East Asia. Comprehensive Guidelines for Prevention and Control of Dengue and Dengue Hemorrhagic Fever, Revised and Expanded Edition. WHO-SEARO 2011. (SEARO Technical Publication Series No. (60), 2011.
4. Shivbalan S, Anandnathan K, Balasubramanian S, Datta M, Amalraj E. Predictors of spontaneous bleeding in dengue. *Indian J Pediatric*. 2004; 71(1):33-6.
5. Kaur P, Kaur G. Transfusion support in patients with dengue fever. *Int J Appl Basic Med Res*. 2014; 4(Suppl 1):S8-S12.
6. Kurukularatne C, DimatatacF, Teo DL, Lye DC, Leo YS. When less is more: Can we abandon prophylactic platelet transfusion in dengue fever? *Ann Acad Med Singapore*. 2011; 40:539-45.
7. Galel SA, Malone JM, Viele MK. Transfusion medicine. In: Greer JP, Foerster J, Lukens JN, Rodgers GM, Paraskevas F, Galder B, editors. Wintrobe's Clinical Hematology. 11th ed. Philadelphia: Lippincott Williams and Wilkins; 2004; 831.
8. Putta Suresh, Yamani Devi, Crams Kumar, Y. Jalapa. Evaluation of the cause in Fever with Thrombocytopenia cases. *J Evidence-based Medicine and Healthcare*. 2015; 2(15): 2134-2137.
9. Rekha M.C, Sumangala B, Ishwarya B. Clinical study of fever with thrombocytopenia. *J Evolution Med and Dent Sci*. 2014; 3(51):11983- 11990.
10. Amita A Gandhi Pankaj J AkhaolKar. Clinical and laboratory evaluation of patients with febrile thrombocytopenia. *National*

- Journal of Medical Research*. 2015; 5(1):43-46.
11. Pankaj B Palange, R B Kulkarni, R K Shrawasti. A study of Clinical profile of patients with dengue fever with thrombocytopenia. *J Recent trends in Science and Technology*. 2015; 13(3):671-675.
 12. Prithivraj Patil, Pranita Solanke, Gayathri Harshe. Clinical Evaluation and Outcome of Patients with Febrile Thrombocytopenia. *Int J Scientific and Research Publications*. October 2014; 4(10):1-3.
 13. Shruthi K Bhalara, Smitha Shah, Hansa Goswami. Clinical and etiological profile of thrombocytopenia in adults. *Int J Medical Sci Public Health*. 2015; 4(1):7-10.
 14. Djamiatun K, Van der Ven AJ, de Groot PG, Faradz SM, Hapsari D, Dolmans WM, et al. Severe dengue is associated with consumption of von Willebrand factor and its cleaving enzyme ADAMTS-13. *PLoS Negl Trop Dis*. 2012; 6:e1628.
 15. Hima Bindu T et al. Study of hepatic involvement in children with dengue infection. *Int J Contemporary Paediatrics*. 2017; 4(6):2012-2014.
 16. Bhattacharjee B, Bhattacharya S, Majumdar D, Chakraborty S, Sardar B et al. An observational study on clinical, Epidemiological and laboratory profile in patients of Dengue Fever. *J Microbiol Exp*. 2016; 5(5): 00161.
 17. Makroo RN, Raina V, Kumar P, Kanth RK. Role of platlet transfusion in the management of dengue patients in a tertiary care hospital. *Asian J Transfusion Sci*. 2007;1(1):4-7.
 18. Sellahewa KH et al. Role of Fresh Frozen Plasma in treating thrombocytopenia in adukts with dengue fever. A prospective randomised double blind study. *Ceylon Med J*. 2008; 53(2):36-40.