



ROLE OF PLATELET TRANSFUSION IN DENGUE PATIENTS WITH BLEEDING TENDENCY IN TERTIARY CARE HOSPITAL

Pathology

Dr Dipali Bhatt Senior Resident

Dr Manushi Parekh Senior Resident

Dr Jitendra Chavada Associate Professor

Dr Shaila N Shah Hod & Professor

ABSTRACT

Introduction: Dengue fever and dengue hemorrhagic fever (1) are usually a benign condition caused by an arthropod borne virus and bleeding is one of the dreaded complications associated with higher mortality in DHF/DSS (1) Dysfunction of platelets are Prothrombotic complications associated with severe cases of dengue. Thus, platelets could be considered cells that are active against the anti DENV immune response. Platelet transfusion is given in those patients who are either bleeding or having other hemorrhagic symptoms along with thrombocytopenia. A Prospective study was conducted of 100 dengue positive patients with bleeding tendency in department of pathology, Government medical college and Sir. T. Hospital, Bhavnagar, Gujarat during period of July 2020 to MAY 2021. The patient who received multiple platelet transfusions showed post transfusion platelet increment of $>0.5 \times 10^5/\text{mm}^3$ from each unit.

KEYWORDS

Dengue, Platelet transfusion, Bleeding

INTRODUCTION

Bleeding in dengue is one of the dreaded complications and associated with higher mortality⁽¹⁾. Dysfunction of platelets is implicated in Prothrombotic complications associated with severe cases of dengue. Factors like mild degree of disseminated intravascular coagulation (DIC), hepatic derangement and thrombocytopenia act synergistically to cause bleeding in dengue patient⁽¹⁾. Platelet transfusion is given in those patients who are either bleeding or having other hemorrhagic symptoms along with thrombocytopenia. Tertiary care hospital has a facility for transfusion so we can study the exact amount of platelet increments after transfusion. Therefore, we can evaluate effectiveness of platelet transfusion in management of dengue patients.

AIM & OBJECTIVES

To evaluate effectiveness and the number of platelets transfusion require for stoppage of bleeding.

MATERIAL AND METHOD

A Prospective study of 100 dengue positive patients and 100 Dengue negative patients with thrombocytopenia from medicine was conducted in department of pathology, Government medical college and Sir. T. Hospital, Bhavnagar, Gujarat during period of July 2020 to MAY 2021.

Inclusion criteria:

Dengue NS1 antigen positive and or IgM antibody positive.

Exclusion criteria:

Idiopathic thrombocytopenic purpura, Aplastic anemia Infection- HIV Myelodysplastic syndromes Drugs- heparin, warfarin Bone marrow failure Cancer Leukemia Exposure Radiotherapy anytime in life Myeloma Post viral: parvo, Hep B/C, EBV, varicella, measles, mumps, rubella, CMV.

RESULTS

During the epidemic of dengue fever, of the 200 clinically suspected dengue cases, 100 cases were positive for dengue serological tests. Among 100 serologically positive dengue cases, 54 (54%) cases were DF, 46 (46%) cases were DHF. For 5 (5%) out of 100 serologically confirmed cases there was no information about the duration of fever in the medical records. 64% patients were males and 36% were females in study group and 43% patients were males and 57% were females in control group. Involvement of all age groups were observed, but most patients were between the age group of 18–29 years is 32 (32%) and 40–49 year is 33 (33%) cases. By comparing control and study group mean and standard deviation result of P value is <0.001 which is statistically significant.

[Number of patients with bleeding complications]

	Age Group (year)				
	18-29 year	30-39 year	40-49 year	50-60 year	>60 year
Hematemesis	20	05	23	13	06
Melena	19	01	16	10	08
Gum bleeding	22	04	26	12	05
Rectal bleeding	13	01	18	10	05
Epistaxis	28	06	25	18	05
Total	102	17	108	63	29

Platelet Count	Number of Patients	Average Number of Platelet Component Used
<5000	13	173
5000-10000	35	377
10000-20000	29	234
20000-30000	06	32
30000-40000	06	18
>40000	11	30
Total	100	864

All the five features of Hemorrhagic manifestations were present in 43 (43%) cases out of 100 dengue cases. 43% case of all the hemorrhagic manifestations occurred in patients with severe thrombocytopenia with platelet count $<0.5 \times 10^5/\text{mm}^3$. 48% patients who had platelet count $<10 \times 10^5/\text{mm}^3$ received multiple platelet transfusions. Among 100 patients, 35% patients received 377 units and 13% patients received 173 units of platelets. 20 patients who had abnormal coagulation profile, received FFP with platelet transfusion. Majority of cases developed thrombocytopenia between the 3rd and 5th day of illness thus most hemorrhagic manifestations occurred between 4th to 6th day. Severe thrombocytopenia with platelet count $<0.5 \times 10^5/\text{mm}^3$ was present in 13 % out of 100 dengue cases. Platelet count between $0.5-10 \times 10^5/\text{mm}^3$ was present in 35% cases. Platelet count $>40 \times 10^5/\text{mm}^3$ was present in 11 % patients. Most of bleeding manifestation happened in patients with platelet count $<10 \times 10^5/\text{mm}^3$ and least bleeding manifestation happened in patients with platelet count is $>40 \times 10^5/\text{mm}^3$. 30 patients who had Hb <7.0 g/dl received packed red cells (PRC) along with platelet transfusion. The patient who received multiple platelet transfusions showed post transfusion platelet increment of $>0.5 \times 10^5/\text{mm}^3$ from each unit. There is significant increase in platelet count and resolution of bleeding complications on each platelet unit transfusion.

DISCUSSION

Makroo et al⁽²⁶⁾ studied 225 serologically confirmed cases and classified 112 (49.8%), 113 (50.2%) patients as DF, DHF respectively

and in our study, it was 54(54%),46 (46%) which is similar⁽²⁶⁾. This study shows that majority of dengue cases (41%) were children with the largest population in the age group of 15–30 years. This is similar to our study and with other studies from Indonesia, Thailand and Myanmar⁽²⁷⁾. In concurrent transmission of several serotypes, primary dengue virus infections are seen in young children, whereas symptomatic dengue generally occurs during secondary dengue virus infections in school age children or young adults⁽²⁸⁾. In this study 53% dengue cases were admitted before day four of their illness, but in the study by **Nimmannitya et al**⁽²⁸⁾ 59% of dengue cases were admitted between 5–7 days of the illness. **Makroo et al**⁽²⁶⁾ recorded 15.11% and **Chairulfatah et al**⁽²⁷⁾ recorded 6% of dengue cases with hemorrhagic manifestation and both observed severe bleeding with platelet count $<0.2 \times 10^5/\text{mm}^3$ ^(26,27). In the present study hemorrhagic manifestations were present with platelet count $<0.5 \times 10^5/\text{mm}^3$ ^(26,27,28). **Makroo et al**⁽²⁶⁾ found 0.8% mortality rate but in the present study the high rate 10% may be due to severe bleeding from rectum. **Makroo et al**⁽²⁶⁾ found 0.8% mortality rate but in the present study the high rate 10% may be due to severe bleeding from rectum. Published data from various institutions^(5,6) and countries have put varying figures as the trigger for platelet transfusion in hospitalized dengue patients. In this study 13% patients who had platelet count $<0.5 \times 10^5/\text{mm}^3$ and 35% patients whose platelet count was between $0.5\text{--}10 \times 10^5/\text{mm}^3$ received multiple platelet transfusions, and whose platelet count was $>40 \times 10^5/\text{mm}^3$ received single unit of platelet transfusion.

CONCLUSION

In all the patients of DF/DHF there is significant increase in platelet count and resolution of bleeding complications on each platelet unit transfusion.

REFERENCES

- Guha-Sapir, D., and B. Schimmer. 2005. Dengue fever: new paradigms for a changing epidemiology. *Emerg. Themes Epidemiol.* 2:1. Harris, E., E. Videia, L.
- Perez, E. Sandoval, Y. Tellez, M. L. Perez, R. Cuadra, J. Rocha, W. Idiaquez, R. E. Alonso, M. A. Delgado, L. A. Campo, F. Acevedo, A. Gonzalez, J. J. Amador, and A. Balmaseda. 2000. Clinical, epidemiologic, and virologic features of dengue in the 1998 epidemic in Nicaragua. *Am. J. Trop. Med. Hyg.* 63:5–11
- Carlos, C. C., K. Oishi, M. T. Cinco, C. A. Mapua, S. Inoue, D. J. Cruz, M. A. Pancho, C. Z. Tanig, R. R. Matias, K. Morita, F. F. Natividad, A. Igarashi, and T. Nagatake. 2005. Comparison of clinical features and hematologic abnormalities between dengue fever and dengue hemorrhagic fever among children in the Philippines. *Am. J. Trop. Med. Hyg.* 73:435–440.
- Guzman, M. G., G. Kouri, J. Bravo, L. Valdes, S. Vazquez, and S. B. Halstead. 2002. Effect of age on outcome of secondary dengue 2 infections. *Int. J. Infect. Dis.* 6:118–124.
- 76Heddl NM, Cook RJ, Timmouth A, Kouroukis CT, Hervig T, Klapper E, et al. A randomized controlled trial comparing standard and low-dose strategies for transfusion of platelets (SToP) to patients with thrombocytopenia. *Blood.* 2009;113:1564–73
- 81Anupam Verma, Prashant Agarwal. platelet utilization in the developing world strategies to optimize platelet transfusion practices. *Transfusion and Apheresis Science* 2009;41(2):145–9. 7. Kumar ND, Tomar V, Singh B, Kela K. Platelet transfusion practice during dengue fever epidemic. *Indian J Pathol Microbiol* 2000;42(1):55–60.
- Guilarte, A. O., M. D. Turchi, J. B. Siqueira, Jr., V. C. Feres, B. Rocha, J. E. Levi, V. A. Souza, L. S. Boas, C. S. Pannuti, and C. M. Martelli. 2008. Dengue and dengue hemorrhagic fever among adults: clinical outcomes related to viremia, serotypes, and antibody response. *J. Infect. Dis.* 197: 817–824.
- Wills, B. A., E. E. Oragui, A. C. Stephens, O. A. Daramola, N. M. Dung, H. T. Loan, N. V. Chau, M. Chambers, K. Stepniowska, J. J. Farrar, and M. Levin. 2002. Coagulation abnormalities in dengue hemorrhagic fever: serial investigations in 167 Vietnamese children with dengue shock syndrome. *Clin. Infect. Dis.* 35:277–285.
- Mairuhu, A. T., M. R. Mac Gillavry, T. E. Setiati, A. Soemantri, H. ten Cate, D. P. Brandjes, and E. C. van Gorp. 2003. Is clinical outcome of dengue-virus infections influenced by coagulation and fibrinolysis? A critical review of the evidence. *Lancet Infect. Dis.* 3:33–41.
- Limon-Flores, A. Y., M. Perez-Tapia, I. Estrada-Garcia, G. Vaughan, A. Escobar-Gutierrez, J. Calderon-Amador, S. E. Herrera-Rodriguez, A. Brizuela-Garcia, M. Heras-Chavarria, A. Flores-Langarica, L. Cedillo-Barron, and L. Flores-Romo. 2005. Dengue virus inoculation to human skin explants: an effective approach to assess in situ the early infection and the effects on cutaneous dendritic cells. *Int. J. Exp. Pathol.* 86:323–334.
- Wu, S. J., G. Grouard-Vogel, W. Sun, J. R. Mascola, E. Brachtel, R. Putvatana, M. K. Louder, L. Filgueira, M. A. Marovich, H. K. Wong, A. Blauvelt, G. S. Murphy, M. L. Robb, B. L. Innes, D. L. Birk, C. G. Hayes, and S. S. Frankel. 2000. Human skin Langerhans cells are targets of dengue virus infection. *Nat. Med.* 6:816–820.
- Durbin, A. P., M. J. Vargas, K. Wanionek, S. N. Hammond, A. Gordon, C. Rocha, A. Balmaseda, and E. Harris. 2008. Phenotyping of peripheral blood mononuclear cells during acute dengue illness demonstrates infection and increased activation of monocytes in severe cases compared to classic dengue fever. *Virology* 376:429–435.
- Boonnak, K., B. M. Slike, T. H. Burgess, R. M. Mason, S. J. Wu, P. Sun, K. Porter, I. F. Rudiman, D. Yuwono, P. Puthavathana, and M. A. Marovich. 2008. Role of dendritic cells in antibody-dependent enhancement of dengue virus infection. *J. Virol.* 82:3939–3951.
- Ho, L. J., M. F. Shaio, D. M. Chang, C. L. Liao, and J. H. Lai. 2004. Infection of human dendritic cells by dengue virus activates and primes T cells towards Th0-like phenotype producing both Th1 and Th2 cytokines. *Immunol. Investig.* 33:423–437.
- Ho, L. J., J. J. Wang, M. F. Shaio, C. L. Kao, D. M. Chang, S. W. Han, and J. H. Lai. 2001. Infection of human dendritic cells by dengue virus causes cell maturation and cytokine production. *J. Immunol.* 166:1499–1506.
- Kwan, W. H., A. M. Helt, C. Maranon, J. B. Barbaroux, A. Hosmalin, E. Harris, W. H. Fridman, and C. G. Mueller. 2005. Dendritic cell precursors are permissive to dengue virus and human immunodeficiency virus infection. *J. Virol.* 79:7291–7299.
- Libraty, D. H., S. Pichyangkul, C. Ajariyakhajorn, T. P. Endy, and F. A. Ennis. 2001. Human dendritic cells are activated by dengue virus infection: enhancement by gamma interferon and implications for disease pathogenesis. *J. Virol.* 75:3501–3508.
- Blackley, S., Z. Kou, H. Chen, M. Quinn, R. C. Rose, J. J. Schlesinger, M. Coppage, and X. Jin. 2007. Primary human splenic macrophages, but not T or B cells, are the principal target cells for dengue virus infection in vitro. *J. Virol.* 81:13325–13334.
- Dejana, E., E. Tournier-Lasserre, and B. M. Weinstein. 2009. The control of vascular integrity by endothelial cell junctions: molecular basis and pathological implications. *Dev. Cell* 16:209–221.
- Huerre, M. R., N. T. Lan, P. Marianneau, N. B. Hue, H. Khun, N. T. Hung, N. T. Khen, M. T. Drouet, V. T. Huong, D. Q. Ha, Y. Buisson, and V. Deubel. 2001. Liver histopathology and biological correlates in five cases of fatal dengue fever in Vietnamese children. *VirchowsArch.* 438:107–115.
- Kyle, J. L., P. R. Beatty, and E. Harris. 2007. Dengue virus infects macrophages and dendritic cells in a mouse model of infection. *J. Infect. Dis.* 195:1808–1817.
- Marchette, N. J., S. B. Halstead, W. A. Falkler, Jr., A. Stenhouse, and D. Nash. 1973. Studies on the pathogenesis of dengue infection in monkeys. 3. Sequential distribution of virus in primary and heterologous infections. *J. Infect. Dis.* 128:23–30.
- Espina, L. M., N. J. Valero, J. M. Hernandez, and J. A. Mosquera. 2003. Increased apoptosis and expression of tumor necrosis factor-alpha caused by infection of cultured human monocytes with dengue virus. *Am. J. Trop. Med. Hyg.* 68:48–53.
- Chao, Y. C., C. S. Huang, C. N. Lee, S. Y. Chang, C. C. King, and C. L. Kao. 2008. Higher infection of dengue virus serotype 2 in human monocytes of patients with G6PD deficiency. *PLoS One* 3:e1557.
- Nishioka, K. 1974. Serum complements level in dengue hemorrhagic fever. *Allerg. Immunol. (Leipzig)* 21:385–392.
- Makroo RN, Raina V, Kumar P, Kanth RK. Role of platelet transfusion in the management of dengue patients in a tertiary care hospital. *Asian J Transfus Sci.* 2007;1:4–7.
- Alex chairulfatah, Djatnika setiabudi, Ridad Agoes, Robert colebunders. Thrombocytopenia and platelet transfusion in dengue hemorrhagic fever and dengue shock syndrome. *WHO Dengue Bulletin* 2003;27:138–43. 28. Nimmannitya S, Halstead SB, Cohen SN, Margiotta MR. Dengue and chikungunya virus infection in man in Thailand, 1962/1964. I. Observations on hospitalized patients with hemorrhagic fever. *Am J of tropical medicine and hygiene* 1969;18:954–71.