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RESEARCH ARTICLE

PROPHYLACTIC PLATELET TRANSFUSION IN DENGUE PATIENTS: A RETROSPECTIVE STUDY

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ABSTRACT

Dengue is the most rapidly spreading mosquito-borne viral disease in the world. We conducted a retrospective study know the role of prophylactic platelet transfusion and its misuse in dengue patients. A total of 110 dengue patients who have been platelet transfused were taken in the study. A total of 311 platelet concentrates were transfused, while 70 units of FFP were infused to 41 patients with DHF or DSS. Out of a total of 311 platelet concentrate 131(42.11%) units were prophylacticaly transfused to DF patients who did not manifest bleeding and they were considered as inappropriate platelet transfusion. The reason for platelet transfusion are not based on medical rationale, but as a result of an intense social pressure on the treating physicians by the patients and their relatives. More reasearh is require to address the role of prophylactic platelet transfusion in dengue fever.

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INTRODUCTION

Dengue is the most rapidly spreading mosquito-borne viral disease in the world. In the last 50 years, incidence has increased 30-fold with increasing geographic expansion to new countries and, in the present decade, from urban to rural settings. An estimated 50 million dengue infections occur annually and approximately 2.5 billion people live in dengue endemic countries (Edelman, 2007) Dengue, the most important arbo-viral infection of humans (Dar *et al*., 1999). The incidence has increased dramatically over the last few decades all over the world (WHO, 2010). Dengue is a prevalent mosquito-borne acute viral infection with potential fatal complications caused by an arbovirus transmitted by the vector aedes aegypti (Whitehorn *et al*., 2010). The term "break bone fever" was coined for dengue because of the symptoms of myalgia and arthralgia (Gupta *et al*., 2012). Dengue viruses (DV) comes under family Flaviviridae and there are four serotypes of the virus referred to as DV-1, DV-2, DV-3, and DV-4. DV is a positivestranded encapsulated RNA virus and consists of three structural protein genes which encode the nucleocapsid or core (C) protein, a membrane-associated (M) protein, an enveloped (E) glycoprotein, and seven non-structural (NS) proteins (Gupta *et al*., 2012). All four serotypes can cause the full spectrum of disease from a subclinical infection to a mild self-limiting disease, the dengue fever (DF) and a severe disease that may be fatal, the dengue hemorrhagic fever/dengue shock syndrome (DHF/DSS) (Lee *et al*., 2012). Dengue is globally the most important arboviral infection and threatens an estimated 2.5 billion people worldwide. Thrombocytopenia is commonly observed in dengue infection. This result from both reduced production and increased destruction of platelets (Hober *et al*., 1993). Several workers have observed that the severity of thrombocytopenia does not predict bleeding (Hober *et al*., 2003; Whitehorn *et al*., 2012), and that other factors such as platelet dysfunction and a prolonged duration of shock leading to disseminated intravascular coagulation (DIC) may play an important role. WHO has published guidelines (Dengue, 2009), for treatment of Dengue infection, inappropriate use of blood components in Dengue infection remains a major concern. The first report of dengue in India was in 1946, and soon the whole country was involved with widespread epidemics, which was followed by the endemic prevalence of all the four serotypes of dengue virus. Clinical presentation of DF is characterized by an abrupt onset of fever associated with frontal headache and retroorbital pain, myalgia, arthralgia, vomiting, and weakness. A generalized maculopapular rash appears 1 or 2 days after fever defervescence. Minor hemorrhagic manifestations signs like petechiae may be observed in some patients. DF is generally self-limiting, and most patients recover without complications approximately 10 days after the onset of illness. However,

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some patients develop severe manifestations such as increased vascular permeability and plasma leakage that can lead to death. Signs of spontaneous bleeding are more frequent in severe forms of dengue.5 Dengue patients generally have high levels of cytokines, chemotactic complement anaphylatoxins C3a and C5a, and histamine, which have the capability to induce vascular permeability. Evidence indicates that the endothelium itself plays a prominent role in immune-enhanced pathology, and that leads to increased vascular permeability in DHF and DSS. The detection of NS1 in dengue is the basis of commercial diagnostic assays (Dalrymple *et al*., 2012). Dengue patients can be categorized into the four categories based on their platelet count at the time of admission:

- High risk (platelet count 20,000/cu mm).
- Moderate risk (platelet count between 21,000 and 40,000/cu mm)
- Low risk (platelet count between 41,000 and 100,000/cu mm)
- No risk (platelet count >100,000/cu mm) [11]

The DHS guidelines state that platelet transfusion should be given to patients with platelet count <20000/cumm (Dalrymple, 2012). The optimal number of platelets in a prophylactic platelet transfusion is controversial. A standard dose for adults is considered to be approximately 3×10^{11} to 6×10^{11} platelets. Prophylactic platelet transfusion can result in various risks such as alloimmunization, platelet refractoriness, allergic reactions, febrile nonhemolytic reactions, bacterial sepsis, and less commonly transfusion-associated acute lung injury (Kurukularatne *et al*., 2011).

MATERIALS AND METHODS

A retrospective study design was conducted in Dr. Ram Manohar Lohiya Combined Hospital Lucknow. A total of 110 patients (65 males and 45 females, median age 30 years, ranging from (15 to 60 years) with Dengue infection (positive for NS1 Antigen), from july to September 2016 were reviewed retrospectively. Only dengue seropositive (NS1 positive) patients who have undergone platelet transfusion were taken for the study. Patients having a platelet count >20 $x10^3$ /µL in the absence of bleeding manifestations were considered to have received inappropriate platelet transfusion. A value of more than 1.5 times the control for PT and aPTT were considered abnormal for the assessment of coagulopathy. To assess the effectiveness of component transfusion, median percentage change (MPC) (Lum *et al*., 2003), in platelet count were calculated as follows.

Platelet MPC = post transfusion platelet count (median) / pre transfusion level

The main objective was to determine whether prophylactic platelet transfusion is necessary and appropriate in dengue patients who have no bleeding manifestations.

RESULTS

A total of 110 dengue patients who have been platelet transfused were taken in the study. A total of 311 platelet concentrates were transfused, while 70 units of FFP were infused to 41 patients with DHF or DSS. No coagulation derangement was seen in DF patients, however, of 41 patients belonging to DHF and DSS, 20 (48%) had an abnormal coagulation profile. After FFP transfusion they show good clinical improvement. Out of a total of 311 platelet concentrate 131(42.11%) units were prophylacticaly transfused to DF patients who did not manifest bleeding and their platelet count is >20000/µL, they were considered as inappropriate platelet transfusion.

Fig. 1. Common Clinical features of Dengue infection

Clinical feature	Number of cases
Fever	110
Abdominal pain	73
Dyspepsia	80
Enteritis	60
Pleural effusion	20
Ascites	25
Rash	20
Bleeding	13
Dizziness	2

Fig. 1. Pre transfusion platelet counts

Platelet count	Dengue fever	Dengue hemorrhagic fever	Dengue shock syndrome
<20000	29	18	4
20000-40000	30	9	6
>40000	10	3	1

Fever was the most common clinical presentation noted in all patients during the time of admission.

DISCUSSION

In the present study 110 patients who were platelet transfused 69 (62.72%) were prophylactically transfused and the remaining 41 (37.27%) had bleeding manifestations and were therapeutically transfused. Fever, gastritis and hemorrhagic manifestations were the most common presenting features observed. The etiology of thrombocytopenia in Dengue infection is multifactorial. Bone marrow suppression (Murge *et al*., 1998), destruction of megakaryocytes (Lin *et al*., 1989) and the formation of anti-platelet antibodies (Lin *et al*., 2001) are the possible mechanisms postulated. We found no correlation between platelet count and bleeding in Dengue infection. In our study, 18 patients (16.36%) of those who were platelet transfused were in the platelet range of more than 40,000 whereas in Makroo *et al* study the majority of dengue cases who were platelet transfused was between 20,000 and 40,000. Pallavi *et al*. reported 36.6% of dengue patients to have been inappropriately transfused platelets. Studies conducted by Chaudhary *et al*. and Kumar *et al*. showed the patients transfused platelets inappropriately were 21.5% and 56.2%, respectively (Chaudhary *et al*., 2006). There was no significant difference between the male and female group among those who were prophylactically and therapeutically transfused. Mass media play a very important role in hyping up the role of platelet transfusion in dengue patients. Dengue patients get admitted to the hospital for the sole reason of platelet transfusion after reading these unproven reports from the media. The reason for platelet transfusion are not based on medical rationale, but as a result of an intense social pressure on the treating physicians by the patients and their relatives (Makroo *et al*., 2007). Kumar *et al*. also observed that the increased use of platelet transfusion were mostly due to a panic reaction during the epidemic of DF (Whitehorn *et al*., 2012). Clinician awareness is low in not knowing the more risk

associated with platelet transfusion than the benefits of it. Randomized controlled trials conducted by Mohammed *et al*. revealed that Platelet transfusion, despite increasing platelet count in half the recipients, neither stopped the progression to severe bleeding nor shortened the time to cessation of bleeding. This proves that a high baseline platelet count and a successful platelet transfusion cannot prevent progression to severe bleeding (Krishnamurti *et al*., 2001).

Conclusion

Platelet transfusion could have been avoided in 57.97% of the dengue patients. Irrational use of platelets will put the patient at a huge risk from transfusion-transmitted infections as well as transfusion-related adverse events. In developing countries, platelet transfusion practices vary between clinicians, hospitals, and regions. There should be a clear set of guidelines regarding the use of platelets in dengue and proper co-ordination among clinicians and transfusion medicine specialist would be helpful in promoting rational use of platelets. Studies suggested that risk factors for bleeding in dengue included degree of thrombocytopenia (Trung *et al*., 2012) older age (Wichmann *et al*., 2001), female gender (Chamnanchanunt *et al*., 2012), high hematocrit and elevated APTT (Tee *et al*., 2009) and high absolute lymphocyte count [22]. While low platelet count was not associated with bleeding in dengue in our study, several correlations for bleeding were identified in our study. They are the presence of fever on the day of platelet count<20000 /mm^3, low white cell count and higher neutrophil proportion. Identification and analysis of other risk factors may contribute to the development of a bleeding risk calculator for the management of dengue patients. There were limitations to our retrospective study.

The lack of randomization may have resulted in treatment bias since the decision to transfuse platelets prophylactically was solely based on treating physician's decision. There were low numbers of severe clinical outcomes such as ICU admission and death in our cohort. Hence the effect of platelet transfusion on these outcomes could not be determined reliably. Although total blood count, RFT and LFT, PT/APTT were done on admission and Platelet count was repeated at least daily, further investigations were performed only when clinically indicated. Our retrospective study showing a lack of efficacy of prophylactic platelet transfusion in the prevention of bleeding in adult dengue with platelet count<20000 /mm^3. It resulted in slower platelet recovery and longer hospital stay. We currently reserve platelet transfusion in dengue fever to those with clinically significant bleeding manifestations. This will reduce the use of precious blood products and associated risks of transfusion. The reason for platelet transfusion are not based on medical rationale, but as a result of an intense social pressure on the treating physicians by the patients and their relatives (Makroo, 2007). More reasearh is require to address the role of prophylactic platelet transfusion in dengue fever.

REFERENCES

Chamnanchanunt, S., Kanagaraj, D., Thanachartwet, V., Desakorn, V., Rojnuckarin, P. 2012. Early predictors of clinically significant bleeding in adults with dengue infection. *Southeast Asian J Trop Med Public Health,* Jul; 43940:890–9.

Chaudhary, R., Khetan, D., Sinha, S., Sinha, P., Sonker, A., Pandey, P., *et al*. 2006. Transfusion support to dengue patients in a hospital based blood transfusion service in north India. *Transfus Apher Sci.,* 35:239-44.

Dalrymple, N.A., Mackow, E.R. 2012. Endothelial cells elicit immune-enhancing responses to dengue virus infection. *J Virol,* 86:6408-15.

Dar, L., Broor, S., Sengupta, S., Xess, I., Seth, P. 1999. The first major outbreak of Dengue hemorrhagic fever in Delhi, India. *Emerg Infect Dis.,* 5:589–90.

Dengue: 2009. Guidelines for diagnosis, treatment, prevention and control -- New edition- WHO.

Edelman, R. 2007. Dengue vaccines approach the finish line. Clinical Infectious Diseases, 45(Suppl 1):S56–S60.

Gupta, N., Srivastava, S., Jain, A., Chaturvedi, U.C. 2012. Dengue in India. *Indian J Med Res*., 136:373-90.

Hober, D., Poh, L., Robin, B., Gestas, P., Chungue, E., Granic, G, *et al*. 1993. Serum levels of tumor necrosis factor-alfa, interleukin 6 and interleukin 1 beta in dengue infected patients. *Am. J. Trop. Med. Hyg.,* 48:324–31. [7] Lum LCS, Latif MEA, Goh AYT, Chan PWE, Lam SK. Preventive transfusion in Dengue shock syndrome – is it necessary? *J Pediatr.,* 143:682–4.

Krishnamurti, C., Kalayanarooj, S., Cutting, M.A., Peat, R.A., Rothwell, S.W., Reid, T.J., *et al*. 2001. Mechanisms of hemorrhage in dengue without circulatory collapse. *Am J Trop Med Hyg*., 65:840-7.

Kumar, N.D., Tomar, V., Singh, B., Kela, K. 2000. Platelet transfusion practice during dengue fever epidemic. *Indian J Pathol Microbiol,* 43:55-60.

Kurukularatne, C., Dimatatac, F., Teo, D.L., Lye, D.C., Leo, Y.S. 2011. When less is more: Can we abandon prophylactic platelet transfusion in Dengue fever? *Ann Acad Med Singapore,* 40:539-45.

Lee, I.K., Liu, J.W., Yang, K.D. 2012. Fatal dengue hemorrhagic fever in adults: Emphasizing the evolutionary pre-fatal clinical and laboratory manifestations. PLoS Negl Trop Dis., 6:e1532.

Lin, C.F., Lei, H.Y., Liu, C.C., Liu, H.S., Yeh, T.M., Wang, S.T., *et al*. 2001. Generation of IgM anti-platelet autoantibody in dengue patients. *J. Med. Virol*, 63:143–9.

Lin, S.F., Li, H.W., Chang, C.S., Yen, J.H., Chin, T.P. 1989. Hematological aspects of Dengue fever. Kaohsiung, *J. Med. Sci.*, 5: 12–6.

Lum, L.C.S., Latif, M.E.A., Goh, A.Y.T., Chan, P.W.E., Lam, S.K. 2003. Preventive transfusion in Dengue shock syndrome – is it necessary? *J Pediatr,* 143:682–4

Makroo, R.N., Raina, V., Kumar, P., Kanth, R.K. 2007. Role of platelet transfusion in the management of dengue patients in a tertiary care hospital. *Asian J. Transfus Sci*., 1:4-7

Murge, B., Cassar, O., Deparis, X., Gurgon, M., Chungue, E. 1998. Implication of macrophage inflammatory proteins 1 alpha in the inhibition of human hematopoetic progenitor growth by Dengue virus. *J Gen Virol.,* 79:1889–93.

Tee, H.P., How, S.H., Jamalludin, A.R., Safhan, M.N., Sapian, M.M., Kuan, Y.C., Sapari, S. 2009. Risk factors associated with development of dengue haemorrhagic fever or dengue shock syndrome in adults in Hospital Tengku Apuan Afzan Kuantan. *Med J Malaysia*., Dec; 64(4):316–20. PMID: 20954558

Trung, D.T., Thao, Le, T.T., Dung, N.M., Ngoc, T.V., Hien, T.T., Chau, N.V.T., Wolbers, M., Tam, D.T.H., Farrar, J., Simmons, C., Wills, B. 2012. Clinical features of dengue in a large Vietnamese cohort: intrinsically lower platelet

counts and greater risk for bleeding in adults than children. PLoS Negl Trop Dis, 6:e1679. doi: 10. 1371/ journal.pntd.0001679 PMID: 22745839

Whitehorn, J., Farrar, J. 2010. Dengue. *Br Med Bull.,* 95:161-73

Whitehorn, J., Rodriguez Roche, R., Guzman, M.G., Martinez, E., Gomez, W.V., Nainggolan, L., *et al*. 2012. Prophylactic platelets in dengue: Survey responses highlight lack of an evidence base. *PLoS Negl Trop Dis.,* 6:e1716

Wichmann, O., Hongsiriwon, S., Bowonwatanuwong, C., Chotivanich, K., Sukthana, Y., Pukrittayakamee, S. 2004. Risk factors and clinical features associated with severe dengue infection in adults and children during the 2001 epidemic in Chonburi, Thailand. Trop Med Int Health. Sep; 9(9):1022–9. PMID: 15361117

World Health Organization. WHO report on global surveillance of epidemic prone infectious diseases.

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