

Dengue fever and thrombocytopenia – A prospective Observational Study at Tertiary Care Centre

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ABSTRACT

Background: Dengue fever is one of the commonest diseases in tropical countries and carries significant morbidity and mortality. Thrombocytopenia (low platelets) is one of the very common manifestations in case of dengue infection. Platelet transfusion in dengue always remains controversial. **Objective:** Present study was conducted to study precise criteria and transfusion trigger for platelet transfusion in our set-up. **Materials and Methods:** This study was conducted on 112 serologically antibody positive confirmed dengue patients admitted in a Hospital, Powai, Mumbai, between 1st of August to 30th October 2017. The age groups of the included patients were within 20-50 years and did not have any co morbidity and were diagnosed at OPD. Indication for hospitalization includes high grade fever ($>101^{\circ}$ F) and platelet counts less than 100,000 along with other viral prodromal symptoms. Clinical data, reports of laboratory investigations, platelets requirements and data obtained from daily follow-up and record sheets were analyzed. **Results:** In the serologically positive confirmed cases, the prevalence of thrombocytopenia (count $<100,000/\text{mm}^3$) was 97% on admission and there was no bleeding recorded in any patient. Out of 112 serologically confirmed dengue cases, only 1 ($<1\%$) patient of dengue received platelet transfusion whose platelet counts were $<7000/\text{mm}^3$ and he had petechiae all over the body. Total 9 patients had platelet count $<10000/\text{mm}^3$ (8.03%), 28 (25%) patients had platelet count $<20,000/\text{mm}^3$, 52 (46%) had a platelet counts $<40,000/\text{mm}^3$ while total 79 (70.53%) patients had platelet counts $<50,000/\text{mm}^3$. In the study population, 28 (25%) patients had platelet count $<20,000/\text{mm}^3$ and 9 (8.03%) patients had platelets count $<10000/\text{mm}^3$, only 1 patient had petechiae; hence platelet transfusion was given. For all other patients who had platelet counts $<20,000/\text{mm}^3$, their clinical parameters were monitored strictly and frequent manual platelet counts were done. These patients were not given any transfusion. **Conclusion:** This study suggests that bleeding due to thrombocytopenia in case of dengue fever is not a common occurrence especially, in otherwise healthy adult or middle aged patients. Those with no or minimum co morbidities and strict monitoring of symptoms are required to preserve the resources and to avoid unwanted platelet transfusions. Platelet count should not be a bench mark for someone to transfuse the platelet. Signs of bleeding, other co-morbid factors and clinical parameters should be taken in to consideration before starting platelet transfusions.

Key words: Dengue, platelet count, thrombocytopenia, platelet transfusion

Dengue fever (DF) is one of the commonest diseases in tropical countries and carries significant morbidity and mortality if goes unrecognised or not taken care properly. DF, dengue haemorrhagic fever (DHF), and Dengue Shock Syndrome (DSS) have emerged as a global public health problem in

recent decades. The South-East Asian countries such as India, Indonesia, Myanmar, and Thailand are at the highest risk of DF/DHF accounting for nearly half of the global risk due to tropical climates and sanitary habits. Thrombocytopenia (low platelets) is one of the commonest findings in case of dengue infection. Platelet transfusion in

dengue always remains controversial and there are no strict guidelines about when to transfuse the platelets, in case of dengue with thrombocytopenia. Bleeding in case of DF is one of the most severe complications and is associated with higher morbidity and mortality in DHF/DSS. Bleeding manifestations are highly variable and many of the times does not correlate with the laboratory findings in the coagulation profile like platelet counts, activated partial thromboplastin time (APTT), prothrombin time (PT), international normalized ratio (INR) etc. Factors like mild degree of disseminated intravascular coagulation (DIC), hepatic dysfunction and low platelets act synergistically to cause bleeding in dengue patient [1]. Severe bleeding is related to severe thrombocytopenia [2].

Platelet transfusion is given only to those patients who is either bleeding or having other complications or haemorrhagic symptoms due to low platelets. Platelet count should not be a bench mark for someone to transfuse the platelet counts like always happens but signs of bleeding; other co-morbid factors and clinical parameters should be taken in to consideration before starting platelet transfusion. We have conducted the study with an aim to show complications in a patients with lower than 10000 platelet counts and the need of blood transfusion.

METHODS

This prospective observational study was conducted on serologically proven dengue patients who were admitted in a hospital in Powai, Mumbai, between 1st August 2017 and 30th September 2017. After getting the informed consent and ethical committee approval and as per the laid down inclusion criteria, 112 confirmed dengue patient with clinical symptoms and fulfilling the case definition criteria of DF and DHF of WHO3, were included in this study and followed up during their hospital stay. Excluding criteria were the dengue patients having age more than 50 years or any co-morbidities or platelet counts $>100,000/\text{mm}^3$.

Clinical data were collected through interviewing the patients or their attendants/relatives and careful physical examination of the patients conducted by the physician. Reports of laboratory investigations, dengue antibodies, platelet requirements and data obtained from daily follow-up details, were analyzed. All the patients were admitted through OPD who were within 20-50 years of age, having high grade fever ($>101^\circ \text{F}$), having Dengue IgM positive with platelet counts $<100,000/\text{mm}^3$.

RESULTS

Of the 112 serologically positive (positive for anti-dengue IgM antibodies) in the study, all cases falls in the category of DHF if we take the platelet as a criteria for classification of dengue here as per the WHO guidelines [3]. The

involvement of all age groups, especially an adult predominance, was observed. All the patients had stable vitals except fever and there was no evidence of any hemorrhagic shock in any of the patient. The mean age of the dengue patient was 27 years and the most belonged to the 21-30 year age group, which included 73 patients (65.17%). Platelet count of $<100,000/\text{mm}^3$ was found in 112 (100%) patients and haematocrit value of $>45\%$ was found in 32 patients (28.57%) at the time of admission. Hemorrhagic or bleeding manifestations were present in only 1 ($<1\%$) patients of dengue infection, which mainly included petechiae and small echmyotic patches over the lower limbs. Any other bleeding manifestations like epistaxis, hematemesis, melena, gum bleeding, etc., were not noticed in any of the patients. Only 1 among the 112 serologically confirmed patients ($<1\%$) received platelet transfusion therapy.

In the serologically confirmed cases, the prevalence of thrombocytopenia was 97% on admission and no bleeding was recorded in any patient. Out of 112 serologically confirmed dengue cases, only 1 patient (1%) of dengue received platelet transfusion whose platelet counts were $<7000/\text{mm}^3$ and he had petechiae all over the body. Total 9 patients had platelet count $<10,000/\text{mm}^3$ (8.03%), 28 patients (25%) had a platelet count $<20,000/\text{mm}^3$, 52 (46%) had a platelet counts $<40,000/\text{mm}^3$ while total 79 (70.53 %) patients had platelet counts $<50,000/\text{mm}^3$. Out of 28 patients with a platelet count $<20,000/\text{mm}^3$, and 9 patients platelets count $<10000/\text{mm}^3$, only one patient had petechiae; hence, platelet transfusion was given. For all other patients who have platelet counts $<20,000/\text{mm}^3$, their clinical parameters were monitored strictly and frequent manual platelet counts were done and no transfusion was given to any of these patients.

All the patients recovered fully and were discharged within 2-3 days of their admission. The platelet counts had increased considerably during their stay in hospital and the average platelet counts of the patients at discharge were around $75,000/\text{mm}^3$ with persistent rising trends of the platelets and stable hemodynamic. Besides platelet transfusion, no fresh frozen plasma (FFP) and packed red blood cell (PRBC) were transfused to any of the dengue patients.

There was only one patient who was suffering from vivax malaria along with dengue fever. No patients died during hospitalization (mortality rate 0%). No patient had any clinical manifestations like septicaemia, or multi-organ failure in other studies. Another finding in our study is that we treated all patients with only antacids, antiemetic, IVF, multivitamins and paracetamol. No patient in this study received any of the antibiotics. Only one patient who had vivax malaria was given anti malarial but no antibiotics. There are studies where many people have given

antibiotics and shown some benefit while our study clearly shows that no antibiotics are required in cases of dengue management and it does not change the outcome of the patients.

DISCUSSION

Dengue fever is a major public health problem in many of the tropical countries like India. Mumbai is one of the big cities in India where, dengue is endemic. This study showed that the majority of dengue cases were adult with the largest proportion in the age group of 21-30 years. This is in accordance with the findings of Pervin et al [4]. Thrombocytopenia was found in 100% of the confirmed cases on admission; this prevalence is comparable with the findings of Chairulfatah et al. who found a similar incidence of 83% in hospitalized dengue patients [2]. Unlike other findings reported Shivbalan et al. and Chairulfatah et al. in which, significant bleeding in patients with thrombocyte count $<15,000 - 20000/\text{mm}^3$, in our study there is no significant bleeding in any of the patients with platelet counts even $<10000/\text{mm}^3$ [1,2].

Published data from various institutions [5-7] and country have put varying figures as the trigger for platelet transfusion in hospitalized dengue patients. The DHS guidelines stipulate that platelet transfusion should be given to patients with platelet count $< 20,000/\text{mm}^3$. In our study, only 1 patient received platelet transfusion which is unlike other earlier studies. Many times the prescription for blood components are not based on medical rationale, but as a response to an intense social pressure on the treating physicians by the patients and their relatives. Many of the times, there are inappropriate platelet transfusions even if the patients' platelet count is $>20,000/\text{mm}^3$ [8].

Some studies have tried to make the appropriate guidelines to trigger for blood or platelet transfusion in case of DF where again, platelet transfusion is advised if the platelet is less than 10000 even if there is no sign of bleeding [9- 11] A restrictive strategy for platelet transfusion based on clinical features and low platelet count thresholds proved to be feasible and safe for adult dengue patients [10]. As per the WHO guidelines, patient who are having counts $<10,000/\text{mm}^3$, comes under the category of high risk and frequent monitoring of the platelets apart from close monitoring of the vital signs are mandatory [3]. While many other people had stressed on the role of platelet transfusion even if the platelet counts are more then 10- 20000/ mm^3 just to be on safer side [8,9,11].

Our study aim was to tell all the clinician is that platelet count is not the trigger for blood transfusion so we should stop counting the numbers to decide about the

platelet transfusion. Similar to our study another study was published from Bangladesh also showed similar outcomes where, only one patient with platelet counts $<10,000/\text{mm}^3$ has undergone blood transfusion [12]. As per WHO criteria, all dengue patients can be categorized as per the risk, into the high, moderate, low and no risk patients based on their platelet count at the time of hospitalization. The high-risk category patients should be given priority and the treating physician should take decision for platelet transfusion. Moderate risk patients should be observed carefully and platelet is transfused only if they have any haemorrhagic manifestations. Low risk patients should not be given any platelet transfusion and should be managed on intravenous fluids and supportive therapy.

Makroo et al. [11] noted that many times the prescription for the platelet are not based on medical rationale, but as a response to an intense social pressure on the treating physicians by the patients and their relatives. Kumar et al. [13] also observed that the demands for platelet transfusion were mostly received as a panic reaction during the epidemic of dengue fever. Observing a fall in platelet count even if the count were above $20 \times 10^9/\text{l}$, the blood prescribing clinicians had sent requisition for platelet transfusion without any specific indications. This actually led to non-availability of platelet in a centre not geared to meet excessive requirements of platelets. The same 'chase' for platelet counts has been mentioned by Ahluwalia [14]. The crux in treatment of dengue patients is maintenance of good hydration, monitoring for any over bleeding and not 'panic' if the platelet count is more than $50,000/\text{cumm}$. This 'syndrome' of chasing platelet count in dengue patients who are otherwise completely asymptomatic and improving can be labelled as 'Dengue panic syndrome'. The efficacy of prophylactic platelet transfusion and the threshold for transfusion is questionable. Platelet transfusions are hardly ever required even with counts as low as $10,000/\text{cumm}$ because the circulating platelets are haematologically active and sufficient to prevent bleeding by thrombocytopenia per se (15). In general, platelet transfusions are given only when there are serious haemorrhagic manifestations.

In our study, we have tried to show that the only trigger for the platelet transfusion is bleeding while platelet counts are not the trigger for platelet transfusion anymore. Many of the times it has been noticed that when platelet transfusion is given out of the fear and patients receive multiple of transfusion since platelet takes almost around 48 hours to stabilise, the patient is exposed to the risk of transfusion associated acute lung injury which increases significant morbidity, hospital stay and even rarely mortality. Also we have tried to show that there is no role of any antibiotics here while treating the dengue fever and misuse of antibiotics should be stopped to overcome the

very important problem of today that is antibiotic resistance.

CONCLUSION

Blood products are limited in developing countries and their use has to be justified. By doing close monitoring of symptoms, we can avoid most of the platelet transfusions in cases of dengue patients. This study highlights that platelet counts are not a trigger for the platelet transfusion even if the counts are less than 10000. Since our study only includes otherwise healthy young and middle aged adults so patient with co-morbidities may need to be very closely monitored for their symptoms specially bleeding.

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