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Correspondence

Haemorrhagic manifestations of dengue fever & their management in a tertiary care hospital in north India

Sir,

Dengue virus infection (DI) has become a serious public health problem. Several outbreaks of DI have been reported from India[1-5]. However, large clinical studies documenting the presentation and management of DI, especially in adults, are scarce. The incidence of haemorrhagic manifestations in DI has varied from 15 to 53 per cent in Indian studies[1,2,5]. Data on the relationship between platelet count and haemorrhagic manifestations in DI are conflicting[1-3,6]. We carried out this study to elucidate the clinical profile of patients with DI with special emphasis on the relationship between haemorrhagic manifestations and thrombocytopenia, and the role of platelet transfusions.

During the months of September to December 2006, 2205 patients admitted with acute febrile illness to Dayanand Medical College and Hospital, Ludhiana, Punjab, India, were included in the study. The provisional diagnosis of DI was based on the presentation of fever of short duration (<15 days) and constitutional symptoms, with or without haemorrhagic manifestations. Blood samples were screened for dengue specific IgM and IgG antibodies, by IgM and IgG Capture ELISA (Panbio diagnostics, Brisbane, Australia), and 366 patients were found to be reactive for dengue antibodies. Medical records of 265 consecutive patients who had positive IgM antibody were analyzed. Patients were grouped into 3 categories- *(i)* dengue fever (DF), *(ii)* dengue haemorrhagic fever (DHF) and *(iii)* dengue shock syndrome (DSS), according to the WHO criteria[7,8]. DF patients were sub-divided into - *(i)* classical DF (CDF) - patients without bleed or with superficial bleed in the form of skin rash/petechiae and; *(ii)* DF with haemorrhagic manifestations (DFHem) -patients having unusual haemorrhagic manifestations.

Among the 265 dengue IgM antibody positive patients, 57 were also IgG antibody positive. They were classified as DF (n=217, 81.9%), DHF (n=36, 13.6%) and DSS (n=12, 4.5%). DF patients were sub classified into CDF (n=178, 82.03%) and DFHem (n=39, 17.97%). The mean age of patients was 31.4 ± 13.8 yr (range 5-80 yr). Maximum number of patients (n=90; 33.9%) were in the age group of 21-30 yr. There were 202 (76.2%) males and 63 (23.8%) females (male: female ratio= 3.2:1). Chi square test and Student's unpaired t test were used for data analysis.

The various presenting symptoms were - fever (100%), myalgias (n=110, 41.5%), haemorrhagic manifestations (n=98, 36.9%), vomiting (n=94, 35.5%), abdominal pain (n=54, 20.4%), headache (n=51, 19.2%), arthralgias (n=18, 6.8%), diarrhoea (n=12, 4.5%) and altered sensorium (n=3, 1.1%). Of the total 98 patients with haemorrhagic manifestations, 50 (51.02%) patients belonged to the DF group; 78 per cent (39/50) of whom had unusual haemorrhagic manifestations. Gastrointestinal tract was the most common site of haemorrhage (n=46/98, 46.9%; melaena 37.8%, haematemesis 12.2%, haematochezia 2.04%), followed by petechiae (n=31, 31.6%), gum bleed (n=19, 19.4%) and epistaxis (n=10, 10.2%).

The mean haemoglobin, haematocrit and platelet count at admission were 13.9 ± 2.5 gm/dl, 40.8 ± 7.3 per cent and 49.3 ± 36.9 x 10^3/µl respectively. Platelet count of less than 100 x 10^3/µl was observed in 241 (90.9%) patients, less than 50 x 10^3/µl in 166 (62.6%), and less than 10 x 10^3/µl in 4 (1.5%) patients. The mean platelet count in DF, DHF and DSS groups was 51.6 ± 38.7, 40.0 ± 26.8 and 34.7 ± 20.5 x 10^3/µl respectively. The mean platelet count in CDF and DFHem subgroups was 50.6 ± 37.9 and 56.4 ± 41.9 x 10^3/µl respectively. Further, the mean platelet count of patients with and without haemorrhagic manifestations was 47.2 ± 34.4 and 50.5 ± 38.4 x 10^3/µl respectively. The characteristics of patients with haemorrhage, who received (n=62/98, 63.3%) and who did not receive platelet transfusions (n=36/98, 36.7%) are shown in Table.

In a systematic review on dengue classification[9], it has been found that some studies had not strictly applied all the four WHO criteria for DHF. The percentage of DHF (including DSS) patients has varied from 15.1 to 49 per cent in Indian studies[1,2,5], while in our study it was 18.1 per cent, using the WHO criteria strictly. The most common site of haemorrhage was gastrointestinal tract (46.9%), in accordance with the findings of other studies[1,3,6]. Statistical analysis of our data showed no association between haemorrhagic manifestations and the degree of thrombocytopenia. In addition, the mean platelet count of patients with and without haemorrhagic manifestations was not significantly different. Other causes of haemorrhage in DI could be coagulation defects, capillary fragility, consumptive coagulopathy and platelet dysfunction[3,10,11]. Poor correlation between haemorrhagic manifestations and the degree of thrombocytopenia in DI has been reported previously[2,4], while two other studies showed that the frequency of bleed was higher at lower platelet counts[3,6] .

Table. Characteristics of patients with haemorrhage who received/ did not receive platelet transfusions

Clinical and laboratory characteristics	Patients who received platelet transfusions (n= 62)	Patients who did not receive platelet transfusions (n=36)
Age (yr)	31.2 ± 13.3	34.3 ± 16.8
Sex (male: female)	49:13	26:10
Initial bleed- Type 1	36 (58.1%)	17 (47.2%)
Type 2	13 (20.9%)	9 (25%)
Type 3	13 (20.9%)	10 (27.8)
Haemoglobin (g/dl)	13.5 ± 3.2	13.1 ± 2.6
Haematocrit (%)	39.3 ± 9.4	39.2 ± 7.9
Platelet count (x 10^3/µl)	37.7 ± 24.1	63.6 ± 42.7
Platelet count ($\log_{10}$)	1.69 ± 0.33	1.49 ± 0.26
Category – DF	29 (46.8%)	21 (58.3%)
DHF	24 (38.7%)	12 (33.3%)
DSS	9 (14.5%)	3 (8.3%)
Platelet transfusions	194	None
Recurrent bleed in hospital#	15 (24.2%)	12 (33.3%)
Hospital stay (days)#	4.4 ± 1.7	3.6 ± 1.5
Mortality#	4 (6.5 %)	3 (8.3%)

Type 1, gastrointestinal bleed, haematuria, haemoptysis, menorrhagia; Type 2, epistaxis, gum bleed; Type 3, skin bleed/petechiae, subconjuctival bleed; #Difference between the two groups for these variables is not statistically significant; DF, Dengue fever; DHF, dengue haemorrhagic fever; DSS, dengue shock syndrome.
Values are expressed as mean ± standard deviation, unless specified

Strict guidelines for the use of platelet transfusions in DI are lacking. In the present study, the decision to transfuse platelets was taken on the basis of overall assessment by the physician, severity of bleed, platelet count and availability of platelet concentrate. A comparison between the patients who received and those who did not receive platelet transfusions showed no significant difference in their outcome in terms of recurrent bleed in hospital, hospital stay and mortality rate. Similar results were reported in a study from Indonesia[6]. The mortality rate in our study (1.9%) was comparable to that reported in other studies[5].

In conclusion, the notable features in this study were appropriate categorization of patients, lack of association between haemorrhagic manifestations and thrombocytopenia, and lack of benefit of platelet transfusions even in patients with haemorrhagic manifestations. Early detection of haemoconcentration and shock, and their prompt management, rather than platelet transfusions, may be the best measures to decrease the cost, morbidity and mortality associated with dengue fever.

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