Characteristics and Management Patterns of Patients Admitted with Fever and Thrombocytopenia to an Acute General Medical Unit in Sri Lanka

Sir,

Dengue infection is one of the major health problems in Sri Lanka. Many outbreaks have been reported in both urban and rural areas since 1970 with progressively greater numbers of dengue patients. During outbreaks, a large numbers of patients with fever and thrombocytopenia are admitted to hospitals and a proportion of them are subsequently found to have dengue fever. Public awareness programmes on dengue direct patients to obtain a blood count if fever persists for more than 3 days; as a result patients often do self-tests, and on finding that their platelet counts are below normal range, either see a doctor or are admitted to hospital. Thus, many patients with fever and thrombocytopenia seek admission to hospital.

In this perspective we sought, in this preliminary study, to determine the characteristics and disease progression in patients admitted to a general medical unit with fever and thrombocytopenia as the primary reason for admission. We retrospectively analyzed all such patients admitted to the University Medical Unit, National Hospital of Sri Lanka over a period of 2 months (May 1, 2009 to the June 30, 2009), during a recent dengue epidemic.

Records of patients admitted to the University Medical Unit of the National Hospital of Sri Lanka (NHSL) with fever were scrutinized, and those patients with thrombocytopenia ($\leq 150 \times 10^9$/L) at the time of admission or thrombocytopenia developing while in ward (within 24 h after admission) were included in our study. Clinical data and data on treatment in ward such as the use of intravenous fluids and platelet-rich plasma (PRP) were collected. Data were analyzed using SPSS 15.0 version®.

Records of 426 patients admitted to the University Medical Unit with short duration fever (2–10 days) were traced from the Medical Records Room at NHSL. Of the 426, 115 fulfilled the inclusion criteria (fever with thrombocytopenia). Twenty-one patients had a final diagnosis other than dengue (leptospirosis, 5; pneumonia, 9; immune thrombocytopenia, 1; diagnosis not determined/recorded in notes, 5).

Ninety-four patients had a final diagnosis of dengue infection, on the basis of clinical features and hematological parameters[1,2] (serology was not routinely available in most cases); these patients characteristics were analyzed. Of them, 58 were male (61%), and the mean age was 31 (range, 13–64) years. The mean duration of fever prior to admission was 4 days (range, 2–7). Apart from fever, muscle pain (67%) was the most frequent symptom at admission, followed by joint pain (61%), and headache (59%). Vomiting (43%) and dizziness (34%) were also common, but were found in less than half of the patients. Seventeen (18%) patients were found to have bleeding manifestations on admission [Table 1]. Sixteen percent of patients were found to have symptomatic postural hypotension (defined as a drop in blood pressure greater than 20mmHg between the supine and seated measurements). Tender hepatomegaly was detected at admission in 13 patients (14%).

We categorized patients into three groups based on their initial platelet counts (i.e., the platelet count on admission) [Table 2]. Overall, 27% of patients had a platelet count below 50×10^9/L while three patients were found to have

Table 1: Bleeding manifestation at admission

Bleeding manifestation	Number of patients (%)
Gum bleeding	4 (4.3)
Bleeding into skin	3 (3.2)
Cannulae site bleeding	2 (2.1)
Hematamesis	4 (4.3)
Malena	4 (4.3)
Hemoptysis	2 (2.1)
Epistaxis	3 (3.2)
Nonmenstrual vaginal bleeding	1 (2.8)
Excessive menstrual loss	1 (2.8)

Table 2: Characteristics of patients categorized according to admission platelet counts

	Platelet count at admission		
	$\leq 50 \times 10^9$/L	$51–100 \times 10^9$/L	$101–150 \times 10^9$/L
Number of patients	25 (27%)	31 (33%)	38 (40%)
Average age (range)	35.12 (16–63)	29.65 (13–62)	30.37 (15–64)
Number of patients with bleeding manifestation at admission	9 (36%)	6 (19%)	2 (5%)
Number of patients with headache at admission	11 (44%)	15 (48%)	29 (76%)
Number of patients with WCC <4×10^9/L at admission	11 (44%)	19 (61%)	14 (37%)
Number of patients with vomiting at admission	9 (36%)	18 (58%)	13 (34%)
Percentage given IV normal saline	96%	91%	90%
Percentage given PRP	36%	13%	8%
Average number of days inward	5	4%	5%
Number of patients diagnosed with DHF	10 (40%)	7 (22.6%)	8 (21.1%)

a count below $10×10^9$/L on admission. The mean platelet count at admission was 85.52 (range, 6–150) $×10^9$/L. The lowest platelet count of patients during their stay ranged from 4 to 132 (mean = 57) $×10^9$/L. The mean hematocrit on admission was 41% (range, 19–53). The lowest platelet count and highest hematocrit were seen on day 5. Bleeding manifestations were seen in 9(36%) of the 25 patients with a platelet count below $50×10^9$/L. Bleeding manifestations were significantly more likely with lower platelet counts ($P<0.008$). However, there was no correlation between initial platelet counts and age, use of intravenous fluids, or length of hospital stay.

The white cell count (WCC) was below $4×10^9$/L in 47% of patients. The lowest recorded WCC at admission was $1.5×10^9$/L (normal range, 4–11 $×10^9$/L) while the mean WCC on admission for all patients was 4.78 (range, 1.5-17.7) $×10^9$/L. The WCC was below $4×10^9$/L in 40% of the patients with platelet count below $50×10^9$/L [Table 2]. Forty-three percent of the patients had a neutrophil count of $<2×10^9$/L (normal range, 2–7.5$×10^9$/L) whereas 55% had lymphopenia (normal range, 1.5-4 $×10^9$/L) on admission.

On the day of admission, alanine transaminase was performed in 24 patients, and 83% of these patients showed levels three times or more above upper limit of normal (normal range ≤40 IU/mL). Aspartate transaminase was performed in 22 patients, and 91% of these patients had levels three times or more above upper limit of normal (normal range ≤40 IU/mL). Six patients with elevated liver transaminases had clinically detectable hepatomegaly at admission.

Based on clinical/hematological diagnostic criteria,[1,2] 25 patients had a final diagnosis of dengue hemorrhagic fever (DHF) while 2 patients were found to have both DHF plus clinical and echocardiographic evidence of myocarditis. The rest was managed as probable dengue. None developed clinical shock, and no fatalities due to dengue were recorded during the study period.

With regards to management, 86(91.5%) patients were given intravenous 0.9% normal saline according to the guideline recommendations.[1] Platelet-rich plasma was used in 16 patients based on the treating physicians decision, though not according to guideline recommendations. The total amount of PRP used per patient ranged between 4 and 34 units. Platelet-rich plasma was used significantly more frequently in patients presenting with admission platelet counts below $50×10^9$/L (36% as opposed 13% and 8% in the other two groups, $P<0.011$) [Table 2]. NB: This analysis was based on platelet counts on admission and not the platelet count at which the decision to give platelets was made, which was in all instances based on the guidelines.[1] Intravenous fluids were given in 92% of patients, and the use of intravenous fluids did not correlate with the hematocrit.

Although dengue infection diagnosed on clinical parameters[2] was the commonest cause of fever with thrombocytopenia, it is noteworthy that other conditions such as pneumonia and leptospirosis could also present with a similar picture. C-reactive protein levels were not performed in patients on admission as the test was not available in the state sector hospitals; we suggest that performing a C-RP test may be helpful in differentiating bacterial sepsis from dengue infection. In a clinical setting where dengue is common, there is tendency among clinicians to assume that fever with thrombocytopenia is dengue fever; failure to detect bacterial sepsis early could have serious consequences, and it is important for clinicians to bear this in mind.

While initial platelet counts predict the likelihood of bleeding manifestations and platelet transfusion, they were not found to correlate with the use of normal saline, or with the duration of hospital stay. Our data were insufficient to determine whether platelet counts correlated with the occurrence of clinical shock. It is noteworthy that a high percentage of patients (92%) were administered intravenous fluids regardless of the hematocrit, not based on guideline recommendations. Also, platelet transfusions may have been used unnecessarily, and certainly not in keeping with the guidelines, since as high a percentage as 21% were given PRP. Our results show that adherence to guidelines is still unsatisfactory, even in tertiary care hospitals. It is possible that this is due to lack of knowledge of the guidelines; indeed, previous studies have also shown that knowledge about dengue guidelines among physicians[3] and junior doctors[4] has been poor. This is an important concern, as guidelines are of little use if treating physicians do not follow them.

Thus, we recommend more careful adherence to the guidelines, in particular with regards to intravenous fluid administration and blood product transfusion. A larger prospective study of clinical characteristics in dengue infection has currently just commenced in our unit. Management algorithms during this study period are based on the current guidelines for the management of dengue fever.[2]

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