ORIGINAL ARTICLE

Spontaneous platelet recovery time in primary and secondary dengue infection in a tertiary care hospital

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Abstract

Objective: To determine the spontaneous platelet recovery time in primary and secondary dengue infection in a tertiary care hospital.

Method: The cross-sectional observational study was conducted at Abbasi Shaheed Hospital, Karachi, from July 2010 to January 2011, and comprised 138 seropositive patients with ages 13 years and above who fulfilled the World Health Organisation criteria of probable dengue infection, and presented with platelet count of <50,000/mm^3 were enrolled. Serology was performed using rapid immunochromatographic assay and enzyme-linked immunosorbent assay with differential detection of immunoglobulin M and G. Spontaneous platelet recovery time (days) in both primary and secondary dengue infection was recorded. SPSS 20 was used for statistical analysis.

Result: Of the total 138, patients, 38(27.5%) had primary infection and 100(72.5%) had secondary infection. Male-to-female ratio was 2.3:1. Among primary and secondary infections, platelet count on presentation was not significantly different (p<0.64). Mean spontaneous platelet recovery time was 3±2.6 days and 3±1.87 days in primary and secondary infection respectively. Higher platelet count at presentation was associated with early recovery time (p<0.033). Of 108(78%) patients who presented with platelet count of 20,000-<50,000/mm^3, platelet count of 36(33.33%) rose to >50,000/mm^3 within 2 days, and 62(57.4%) rose to >50,000 in 3-5 days. . In primary and secondary dengue infections, no statistically significant difference was observed in spontaneous platelet recovery time (-=0.87).

Conclusion: Platelet count at presentation and spontaneous platelet recovery time do not significantly differ in primary and secondary dengue infection.

Keywords: Platelet recovery time, Primary dengue infection, Secondary dengue infection. (JPMA 64: 1380; 2014)

Introduction

Dengue infection has emerged as the most rapidly spreading mosquito-borne viral disease of public health concern affecting tropical and subtropical countries across the globe. In Southeast Asia, including Pakistan, multiple outbreaks of dengue infection have occurred over the past few decades. Clinical manifestation caused by dengue virus ranges from an asymptomatic infection to a self-limiting febrile illness to life-threatening infection characterised by increased capillary permeability and shock.

Higher prevalence of secondary dengue infection is reported in dengue endemic areas and has been shown to be associated with more severe disease areas.[1,2] Thrombocytopenia is a constant laboratory finding in dengue infection. The platelets usually drop to below 100,000/mm^3 in febrile phase or around defervescence and may remain low for the first few days of recovery.[3] Variable degree of thrombocytopenia is observed in both primary and secondary dengue infection. Thrombocytopenia i.e. platelet count <100,000/mm^3 is found to be one of the major reasons for tertiary care referred in both public and private sectors even in uncomplicated dengue. The aim of the present study was to determine the spontaneous platelet recovery (SPR) time in primary and secondary dengue infection. Declining pattern of platelet count often creates an overwhelming response on behalf of the patients and their relatives and results in unnecessary hospitalization and platelet transfusion. Understanding the natural history of SPR time would not only help in clinical management, but also decrease the economic burden in terms of hospitalisation and inappropriate platelet transfusions.

Patients and Methods

This cross-sectional observational analytical inferential study was conducted at the Abbasi Shaheed Hospital, Karachi, from July 2010 to January 2011. According to the inclusion criteria, all patients aged 13 years and above presenting with acute febrile illness (fever for 2-7 days) and fulfilling the World Health Organisation (WHO) case definition criteria of Dengue Fever (DF) and Dengue Haemorrhagic Fever (DHF) were included with random

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purposive sampling. We did not have any study that had SPR time as the outcome, so we enrolled as many patients as we could during our study period.

Patients were enrolled as probable DF cases as per the WHO criteria of probable DF i.e. acute febrile illness with two or more of the following manifestations: headache, retro-orbital pain, myalgia, arthralgia, rash, haemorrhagic manifestations, leukopenia and supportive serology. A positive immunoglobulin M (IgM) antibody test on serum samples collected five or more days after the onset of fever, or occurrence at the same location and time as other confirmed cases of DF. DHF is defined as probable cases of dengue and haemorrhagic tendencies, thrombocytopenia and evidence of plasma leakage i.e. >20% rise in haematocrit or signs of plasma leakage (pleural effusion, ascites or hypo-proteinemia).

Patients with bleeding diathesis, haematological malignancies, cirrhosis, malaria, sepsis and enteric fever were excluded. Patients who received platelet transfusion were also excluded.

As per the admission criteria, during dengue outbreak only those suspected cases of DF were hospitalised who either presented with platelet count of <50,000/mm^3 or who had haemorrhagic magnification at any platelet count. Likewise, all those haemodynamically stable patients whose platelet rose to ≥50,000/mm^3 were discharged. We, therefore, recorded SPR time till platelet counts had risen to 50,000/mm^3.

Serological diagnosis of dengue infection was performed using rapid immunochromatography test (ICT) with qualitative detection of dengue IgM and IgG. Acute plasma sera of all the enrolled patients were collected after 5 days of fever onset. In non-reactive cases, repeat ICT was performed after 3-5 days of first sera (within 12 days of fever onset). Dengue IgM capture enzyme-linked immunosorbent assay (ELISA) was done in some suspected patients to confirm the status. In ICT assay, specimen reacts with dengue antigen coated particles (type 1-4) in the test strip and the mixture is captured by ligand anti-IgM or anti-IgM, forming a visible band. The IgG cut-off in the test strip has been set to detect the high IgG levels characteristic of secondary infection, therefore the primary dengue infection was defined by a visible IgM band without a visible IgG band, whereas, secondary infection was defined by a positive IgG band with or without positive IgM band.

Data was analysed using SPSS 20.0. Mean and standard deviations (SD) were calculated for continuous variables and frequencies were done to determine relationship between different variables. Statistical significance was considered at $p < 0.05$.

Results

Of the patients initially enrolled, 3(2%) had concomitant plasmodium vivax infection and were excluded. The final sample, as such, comprised 138(98%) patients. The maximum number of patients were admitted in September 46(33.3%), October 72(52%), November 9(6.5%) and December 4(2.9%). Overall male-to-female ratio was 2.3:1 with 97 (70%) males and 41 (30%) females. In terms of age, 110 (79.7%) patients belonged to 13-33 group. Among the cases, 38(27.5%) had primary dengue infection and 100(72.5%) had secondary dengue infection (Table-1). The distribution of thrombocytopenia on presentation among cases of primary and secondary dengue infection was also noted (Figure-1).

Table-1: Clinical and laboratory characteristics.

Age (Years)	Total (n=138)	Primary Dengue (n=38)	Secondary Dengue (n=100)	P. Value
13 - 33	110 (79.7%)	28 (73.6%)	82 (82%)	0.461
34 - 53	16 (11.6%)	5 (13%)	11 (11%)	
>53	12 (8.7%)	5 (13%)	7 (7%)	
Fever	138 (100%)	38 (100%)	100 (100%)	-
Bleeding	46 (33.3%)	11 (28.9%)	35 (35%)	(0.55)
Rashes	43 (40.6%)	14 (42.4%)	29 (39.7%)	(0.833)
Abdominal Pain	30 (46.9%)	9 (45%)	21 (47.7%)	(1.0)
Nausea Vomiting	107 (77.5%)	31 (81.6%)	76 (76%)	(0.648)
Headache	22 (27.2%)	8 (30.8%)	14 (25.5%)	(0.605)
Myalgia / Arthralgia	40 (62.3%)	14 (70%)	26 (59.1%)	(0.578)
P/t count on presentation				-
<10,000	7(5.1%)	4(10.5%)	3(3%)	0.064
11 - 20	23 (16.7%)	4 (10.5%)	19 (19%)	
21 - 30	40 (29%)	15 (39.4%)	25 (25%)	
>30	68 (49.2%)	15 (39.4%)	53 (53%)	

Table-2: Platelet recovery time.

Platelet count of Presentation	Recovery time (days)				Total No. of Patients
	≤ 2 days	3 - 5	6 - 8	> 8	
< 10,000/mm^3	0(0)	5(6)	1(9.1)	1(16.7)	7(5.1)
10,000 - < 20,000/mm^3	2(5.3)	16(19.3)	2(18.2)	3(50)	23(16.7)
20,000 - < 30,000/mm^3	9(23.7)	27(32.5)	3(27.3)	1(16.7)	40(29)
>30,000 /mm^3	27(71.1)	35(42.2)	5(45.5)	1(16.7)	68(49.3)
Total number of patients	38(100)	83(100)	11(100)	6(100)	138(100)

P value came out to be 0.033.Value in brackets show percentage.

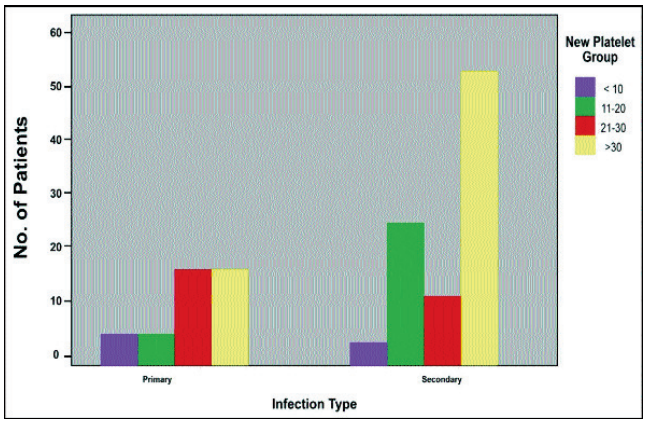

Figure-1: The distribution of thrombocytopenia on presentation among cases of primary and secondary dengue infection.

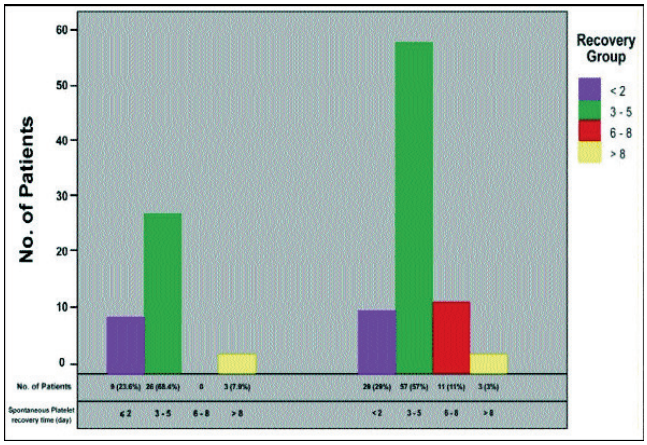

Figure-2: Spontaneous Platelet Recovery time (days) in primary dengue infection and secondary dengue infection.

Platelet count was recorded daily in all patients till the count had risen to 50,000/mm^3. The count of 83 (60%) patients rose to 50,000/mm^3 in 3-5 days' time (Table-2). Higher platelet count at presentation was associated with early recovery time (p<0.03).

Mean platelet count in cohort of -primary dengue infection was 28±13/mm^3 and secondary dengue infection was 31±11/mm^3. Mean SPR time (days) was 3±2.6 days in primary dengue infection and 3±1.87 days in secondary dengue infection (Figure-2). No statistically significant difference was observed in SPR time between primary and secondary dengue infections (p<0.87).

Discussion

In Pakistan significant dengue outbreaks have been witnessed over past the few years. Post-monsoon seasonal trend of dengue outbreaks have been reported in Southeast Asia.[4,5] Our study also supports this seasonal trend, as peak incidence was observed in September and October. The most affected age group with both primary and secondary dengue infection belonged to 13-33 age group (p=0.871). Similar to our findings another study[6] also found no significant statistical difference in age group among primary and secondary dengue infections. In contrast to our findings, one study[7] showed higher percentage of secondary infection in patients >50 years of age.

Serological studies conducted in four provinces of Pakistan identified all four dengue serotypes (DEN1 to DEN4) during multiple outbreaks. In 1994 outbreak of dengue in Karachi, DEN1 and DEN2 were identified, DEN3 was isolated in 2005 outbreak and co-circulation of DEN2 and DEN3 was found in the 2006 outbreak.[8-10] In the 2008 outbreak in Lahore, DEN4, DEN2 and DEN3 were identified, whereas in the 2010 outbreak DEN2 and DEN1 were found.[11,12] This sequential circulation of different serotypes during regular outbreaks in dengue-endemic areas results in an increased rate of secondary dengue infection. The current study also reports high percentage of secondary infection 72% (n=100) in138 patients. Our pervious study from the same tertiary care hospital in Karachi also identified high incidence of secondary infection 83% (n=209).[13] Our findings are consistent with reports from other parts of Southeast Asia. One study[1] found 92% cases of secondary dengue infection, while another[14] reported 79% cases of

secondary dengue infection.

Secondary dengue infection has been shown to be associated with more severe disease,[15] but pathogenesis that lead to severe dengue is not clearly understood. Lack of significant association between disease severity and secondary dengue infection has also been reported.[16,17] We studied clinical manifestations among primary and secondary dengue infection at presentation. No statistically significant difference in clinical presentation was observed among primary and secondary dengue infection. Thrombocytopenia is a common presenting feature is dengue infection. In our cohort of patients, we did not find any significant difference in platelet count on presentation ($p<0.64$) among primary and secondary dengue cases.

Despite the poor correlation between dengue thrombocytopenia and bleeding manifestation,[18,19] most clinicians show an interest in chasing platelet count very closely. Studies have shown inappropriate platelet transfusions in hospitalised patients during dengue outbreaks. A study[20] reported 51% inappropriate platelet transfusion in hospitalised patients, whereas another[21] reported 56% during dengue epidemic in Dehli. We evaluated SPR time in relation to presenting platelet/mm^3. Our study showed that high platelet count at presentation was significantly associated with early recovery time ($p<0.033$). Of 78% (n=108) patients who presented with platelet count of 20,000-<50,000/mm^3, platelet count of 36(33.33%) rose to >50,000/mm^3 within 2 days, and 62(57.4%) rose to >50,000 in 3-5 days. In patinets of primary and secondary dengue infection we did not observe statistically significant difference in SPR time ($p<0.87$).

Conclusion

Out experience of managing patients of uncomplicated primary and secondary dengue cases should be considered to reduce the hospital cost and unnecessary transfusions.

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