

# ASSESSING THE BLEEDING TENDENCIES IN SUBJECTS WITH DENGUE FEVER ADMITTED IN INDIAN HEALTH CARE CENTER

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## ABSTRACT

**Background:** One of the most common causes of fever associated with thrombocytopenia is Dengue which clinically presents itself in various clinical forms but mainly as bleeding tendencies. These bleeding tendencies are the warning signs of reduced platelet counts. Early and prompt intervention in these subjects helps in the reduction of mortality rates in subjects with dengue.

**Aim:** The present clinical study was conducted to assess the bleeding tendencies in subjects with dengue fever admitted to the Indian health care Center.

**Methods:** The present observational clinical study was done on 160 adult subjects of age more than 18 years having a diagnosis of Dengue who were assessed for bleeding tendencies.

**Result:** Most common bleeding tendency seen in the study subjects was petechiae/rashes seen in 94.44% (n=51) subjects followed by gingival bleeding seen in 27.77% (n=15) study subjects, conjunctival suffusion in 22.22% (n=12) study subjects, epistaxis in 14.81% (n=8) study subjects, malena in 9.25% (n=5) study subjects, PR (per-rectal) bleed seen in 7.40% (n=4) study subjects, and hematuria in 5.55% (n=3) study subjects respectively which was the least common bleeding tendency reported in the study subjects. Among all subjects having epistaxis 5% (n=8) were from the platelet range of <50,000 (severe) platelet counts. There were 5.62% (n=9) subjects with conjunctival effusion, 8.75% (n=14) subjects with gingival bleeding, 2.5% (n=4) subjects with PR bleed, 3.12% (n=5) subjects with malena, 1.25% (n=2) subjects with hematuria, and 24.37% (n=39) subjects with petechiae/rashes in the platelet counts of <50,000  $\mu$ l. In the platelet range of 50,000-1 lakhs  $\mu$ l, there were 1.87% (n=3) subjects with conjunctival suffusion, 0.62% (n=1) subject with gingival bleeding, and 7.5% (n=12) subjects with petechiae/ rashes respectively. No subject with bleeding tendencies were in the platelet counts range of  $\geq$ 1 lakh.

**Conclusion:** The present study concludes that one of the major causes of death in dengue subjects is thrombocytopenia in subjects who develop bleeding, manifestations acting as warning signs for platelet assessment, and need frequent evaluation and intervention by platelet transfusion if needed. Timely platelet transfusion in these subjects can help decrease bleeding manifestations and maintain normal platelet counts, hence, reducing mortality rates.

**Keywords:** Bleeding, Dengue, Platelet Counts, Platelet Transfusion, Thrombocytopenia

## INTRODUCTION

An acute viral infection that can lead to death in the affected subjects is Dengue, which is a febrile condition caused by infection caused by the dengue viruses having 4 subtypes and is transmitted by female mosquito bites during blood meal intake by female *Aedes albopictus* or *Aedes aegypti* mosquitoes.<sup>1</sup> Dengue fever usually become asymptomatic within 8-10 days incubation period making it a self-limiting disease, where symptoms usually resolve after 2-7 days. Dengue fever presents itself with the varying clinical picture from being asymptomatic to mid fever to shock syndrome which can be life-threatening. In dengue subjects, the symptoms can be hemorrhagic manifestations, sore throat, malaise, generalized weakness, vomiting, nausea, arthralgia, myalgia, retro-orbital pain, headache, and/or fever.<sup>2,3</sup>

The hemorrhagic manifestations seen in the dengue subjects are Malena, PR bleed, hematuria, conjunctival suffusion, gingival bleeding, petechiae, and/or rashes seen owing to the reduced platelet counts in subjects with dengue fever. World Health Organization (WHO) in 2009 has revised the classification for dengue into different categories as follows: dengue with warning signs and severe dengue and dengue without warning signs.<sup>4</sup> The diagnosis of the virus infection by dengue is made directly by viral component detection and is indirectly diagnosed with serology. Viral antigen or viral nucleic acid detection as a diagnostic tool has high specificity. However, it has a few limitations including its cost and labor sensitivity.<sup>5</sup>

Thrombocytopenia seen in dengue is also associated with various other conditions having associated risks ranging from thrombosis or life-threatening bleed to without risk.<sup>6</sup> In subjects having thrombocytopenia with active bleed, prompt transfusion should be done to maintain platelet counts more than 50,000/ $\mu$ l in various bleeding situations like DIC (disseminated intravascular coagulation), and more than 1,00,000/ $\mu$ l in bleeding of the central nervous system.<sup>7</sup>

Platelet transfusion can be done prophylactically to prevent excessive bleeding or, therapeutically for preparation for an invasive procedure causing bleeding to active bleeding management. Prophylactic transfusion threshold varies based on the clinical situation and subject like in subjects with ITP, no bleeding is seen even at very low platelet counts. Therapeutic transfusion depicts the platelet transfusion for preparation of invasive procedure that can lead to bleeding and transfusion to manage the active bleeding.<sup>8</sup> Prophylactic transfusion is done to stop spontaneous bleeding in afebrile subjects having platelet counts <10,000/ $\mu$ l secondary to the suppression of the bone marrow, whereas, in afebrile and septic subjects, the threshold is higher with counts of 20,000 to 30,000/ $\mu$ l.<sup>9</sup> The present clinical study was conducted to assess the bleeding tendencies in subjects with dengue fever admitted to the Indian health care Center.

## MATERIALS AND METHODS

The present clinical study was conducted to assess the bleeding tendencies in subjects with dengue fever admitted to the Indian health care Center. The study population was comprised of the subjects admitted to the institute with a confirmed diagnosis of dengue fever. After explaining the detailed study designs, informed consent was taken from all the study subjects.

The present study included 160 subjects having confirmed diagnosis of dengue fever from both genders, within the age range of 18-64 years and the mean age of 34.6 $\pm$ 6.28 years. The inclusion criteria for the study were subjects of age 18 years or more, having confirmed diagnosis of dengue fever, admitted to the institute, and were willing to participate in the study. The exclusion criteria for the study were subjects taking drugs that can lead to bleeding manifestations, subjects on blood-thinning medicines, DIC, cirrhosis (drug-induced), and subjects who were not willing to give consent for the study.

After the final inclusion of the study subjects, detailed history was recorded for all the subjects followed by the clinical examination. For the laboratory investigations, the blood was collected from all the study subjects under aseptic and sterile conditions along with the assessment of the complete blood counts to confirm the diagnosis of the dengue fever. All the included study subjects were assessed for bleeding tendencies such as per-rectal bleeding, Malena, hematuria, epistaxis, conjunctival suffusion, gingival bleeding, petechiae, and or rashes.

The collected data were subjected to the statistical evaluation using SPSS software version 21 (Chicago, IL, USA) and one-way ANOVA and t-test for results formulation. The data were expressed in percentage and number, and mean and standard deviation. The level of significance was kept at  $p < 0.05$ .

## RESULTS

The present observational clinical study was conducted to assess the bleeding tendencies in subjects with dengue fever admitted to the Indian health care Center. The present study included 160 subjects having confirmed

diagnosis of dengue fever from both genders, within the age range of 18-64 years and the mean age of 34.6±6.28 years. The demographic and disease characteristics of the study subjects are listed in Table 1. Majority of the study subjects were in the age range of 21-30 years with 31.87% (n=51) subjects followed by 18.75% (n=30) subjects in 41-50 years, 16.87% (n=27) in 31-40 years, 16.25% (n=26) in <20 years, 11.25% (n=18) in 51-60 years, and 3.12% (n=5) in >60 years age range. There were 61.87% (n=99) males and 38.12% (n=61) females in the present study. Bleeding incidence was reported in 33.75% (n=54) subjects in the study. The platelet counts were severe (<50,000  $\mu$ l) in 27.5% (n=44) subjects, 50,000-1 lakhs (moderate) in 44.37% (n=71) subjects, and  $\geq$ 1 lakh (mild) in 28.12% (n=45) subjects respectively.

On assessing the bleeding tendencies in the study subjects, it was seen that the most common bleeding tendency seen in the study subjects was petechiae/rashes seen in 94.44% (n=51) subjects followed by gingival bleeding seen in 27.77% (n=15) study subjects, conjunctival suffusion in 22.22% (n=12) study subjects, epistaxis in 14.81% (n=8) study subjects, Malena in 9.25% (n=5) study subjects, PR (per-rectal) bleed seen in 7.40% (n=4) study subjects and hematuria in 5.55% (n=3) study subjects respectively which was the least common bleeding tendency reported in the study subjects as shown in Table 2.

Concerning the correlation of bleeding tendencies to the platelet counts in the study subjects, it was seen that in all subjects having epistaxis 5% (n=8) were from the platelet range of <50,000 (severe) platelet counts. There were 5.62% (n=9) subjects with conjunctival effusion, 8.75% (n=14) subjects with gingival bleeding, 2.5% (n=4) subjects with PR bleed, 3.12% (n=5) subjects with Malena, 1.25% (n=2) subjects with hematuria, and 24.37% (n=39) subjects with petechiae/rashes in the platelet counts of <50,000  $\mu$ l. In the platelet range of 50,000-1 lakhs  $\mu$ l, there were 1.87% (n=3) subjects with conjunctival suffusion, 0.62% (n=1) subject with gingival bleeding, and 7.5% (n=12) subjects with petechiae/ rashes respectively. No subject with bleeding tendencies was in the platelet counts range of  $\geq$ 1 lakh as depicted in Table 3.

## DISCUSSION

The present observational clinical study was conducted to assess the bleeding tendencies in subjects with dengue fever admitted to the Indian health care Center. The present study included 160 subjects having confirmed diagnosis of dengue fever from both genders, within the age range of 18-64 years and the mean age of 34.6±6.28 years. Majority of the study subjects were in the age range of 21-30 years with 31.87% (n=51) subjects followed by 18.75% (n=30) subjects in 41-50 years, 16.87% (n=27) in 31-40 years, 16.25% (n=26) in <20 years, 11.25% (n=18) in 51-60 years, and 3.12% (n=5) in >60 years age range. There were 61.87% (n=99) males and 38.12% (n=61) females in the present study. Bleeding incidence was reported in 33.75% (n=54) subjects in the study. The platelet counts were severe (<50,000  $\mu$ l) in 27.5% (n=44) subjects, 50,000-1 lakhs (moderate) in 44.37% (n=71) subjects, and  $\geq$ 1 lakh (mild) in 28.12% (n=45) subjects respectively. These demographics and disease characteristics were comparable to the studies of Hottz E et al<sup>10</sup> in 2011 and Gupta G et al<sup>11</sup> in 2012 where authors assessed subjects with comparable demographics and disease characteristics.

Concerning the assessment of the bleeding tendencies in the study subjects, it was seen that the most common bleeding tendency seen in the study subjects was petechiae/rashes seen in 94.44% (n=51) subjects followed by gingival bleeding seen in 27.77% (n=15) study subjects, conjunctival suffusion in 22.22% (n=12) study subjects, epistaxis in 14.81% (n=8) study subjects, Malena in 9.25% (n=5) study subjects, PR (per-rectal) bleed seen in 7.40% (n=4) study subjects and hematuria in 5.55% (n=3) study subjects respectively which was the least common bleeding tendency reported in the study subjects. These results were consistent with the studies of Jacob K Jacob et al<sup>12</sup> in 2017 and Radhika BV et al<sup>13</sup> in 2019 where authors reported similar bleeding tendencies with a comparable incidence as in the present study.

For the correlation of bleeding tendencies to the platelet counts in the study subjects, it was seen that in all subjects having epistaxis 5% (n=8) were from the platelet range of <50,000 (severe) platelet counts. There were 5.62% (n=9) subjects with conjunctival effusion, 8.75% (n=14) subjects with gingival bleeding, 2.5% (n=4) subjects with PR bleed, 3.12% (n=5) subjects with Malena, 1.25% (n=2) subjects with hematuria, and 24.37% (n=39) subjects with petechiae/rashes in the platelet counts of <50,000  $\mu$ l. In the platelet range of 50,000-1 lakhs  $\mu$ l, there were 1.87% (n=3) subjects with conjunctival suffusion, 0.62% (n=1) subject with gingival bleeding, and 7.5% (n=12) subjects with petechiae/ rashes respectively. No subject with bleeding tendencies was in the platelet counts range of  $\geq$ 1 lakh. These results were in agreement with the findings of Changa K et al<sup>14</sup> in 2011 and Sellahewa KH<sup>15</sup> in 2011 where authors reported that lower platelet counts are associated with higher bleeding tendencies in the dengue subjects.

**CONCLUSION**

Within its limitations, the present study concludes that one of the major causes of death in dengue subjects is thrombocytopenia in subjects who develop bleeding, manifestations acting as warning signs for platelet assessment, and need frequent evaluation and intervention by platelet transfusion if needed. Timely platelet transfusion in these subjects can help decrease bleeding manifestations and maintain normal platelet counts, hence, reducing mortality rates. The present study had a few limitations including a small sample size, shorter monitoring period, and geographical area biases. Hence, more longitudinal studies with a larger sample size and longer monitoring period will help reach a definitive conclusion.

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**TABLES**

S. No	Characteristics	Percentage (%)	Number (n)
1.	Mean age (years)	34.6±6.28	
2.	Age range (years)		
a)	<20	16.25	26
b)	21-30	31.87	51
c)	31-40	16.87	27
d)	41-50	18.75	30
e)	51-60	11.25	18
f)	>60	3.12	5
3.	Gender		

a)	Males	61.87	99
b)	Females	38.12	61
<b>4.</b>	<b>Bleeding incidence</b>		
a)	Reported	33.75	54
b)	Not-reported	66.25	106
<b>5.</b>	<b>Platelet counts (<math>\mu</math>l)</b>		
a)	<50,000 (severe)	27.5	44
b)	50,000-1 lakhs (moderate)	44.37	71
c)	$\geq$ 1 lakh (mild)	28.12	45

Table 1: Demographic and disease characteristics of the study subjects

S. No	Bleeding tendencies	Percentage (%)	Number (n=54)
1.	Epistaxis	14.81	8
2.	Conjunctival suffusion	22.22	12
3.	Gingival bleeding	27.77	15
4.	PR (per-rectal) bleed	7.40	4
5.	Malena	9.25	5
6.	Hematuria	5.55	3
7.	Petechiae/rashes	94.44	51

Table 2: Bleeding tendencies in the study subjects

S. No	Bleeding tendencies	<50,000 (severe)		50,000-1 lakhs		$\geq$ 1 lakh	
		%	n	%	N	%	n
1.	Epistaxis	5	8	-	-	-	-
2.	Conjunctival suffusion	5.62	9	1.87	3	-	-
3.	Gingival bleeding	8.75	14	0.62	1	-	-
4.	PR (per-rectal) bleed	2.5	4	-	-	-	-
5.	Malena	3.12	5	-	-	-	-
6.	Hematuria	1.25	2	-	-	-	-
7.	Petechiae/rashes	24.37	39	7.5	12	-	-

Table 3: Correlation of the platelet counts to bleeding tendencies in the study subjects