

Original Research Article

A study on the bleeding tendencies in patients diagnosed with dengue fever in a tertiary care hospital of southern bihar**Sushil Kumar R. Singh¹, Abhilasha Singh², Abhishek Kamendu³, Amit Kumar Ranjan⁴, Amit Kishor^{5*}**¹PG Resident, Department of General Medicine, Narayan Medical College and Hospital, Sasaram, Bihar, India²Associate Professor, Department of Physiology, Narayan Medical College and Hospital, Sasaram, Bihar, India³Associate Professor, Department of General Medicine, Narayan Medical College and Hospital, Sasaram, Bihar, India⁴PG Resident, Department of General Medicine, Narayan Medical College and Hospital, Sasaram, Bihar, India⁵Associate Professor, Department of General Medicine, Narayan Medical College and Hospital, Sasaram, Bihar, India

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Abstract

Background: Dengue is one of the most common cause of fever associated with thrombocytopenia, and it presents clinically in various forms of bleeding manifestations, which acts as a warning sign of declining platelet count values. Timely intervention in such patients help in reducing the mortality rates in patients suffering from dengue. **Methods:** This observational study was carried out on admitted patients in the Department of General Medicine in a tertiary care hospital of Southern Bihar and included 150 patients above the age of 18 years and who were diagnosed to be suffering from dengue. **Result:** The study showed that there was a preponderance in the male patients suffering from dengue, with higher incidence in the age group of 21-30 years. 32.67% patients suffering from dengue manifested with bleeding tendencies, with rash/petechiae being the most common bleeding manifestation. Most of the patients presented with moderate level of thrombocytopenia.

Keywords: Dengue, Thrombocytopenia, Bleeding.

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Introduction

Dengue is an acute viral infection which may lead to fatal consequences. Dengue is a febrile illness which is caused by infection with one of the four dengue virus which is transmitted by bite of female *Aedes aegypti* or *Aedes albopictus* mosquitoes during the taking of a blood meal.^{1,2} Dengue fever was first referred to as “water poison” associated with flying insects in a Chinese medical encyclopaedia in 992 from the Jin dynasty (264-420 AD). The word “dengue” is derived from the Swahili phrase Ka-dinga pepo, meaning “cramp like seizure”. Dengue fever is also known as “Break bone fever”.^[1,2] The term “Break bone fever” was coined by Benjamin Rush because of the accompanying symptoms of myalgia and arthralgia when the first clinical case reported during the epidemic in Philadelphia from 1789 to 1790.^[2] The first epidemic of clinical dengue like illness was recorded in Chennai in 1780 and the first virologically proved epidemic of dengue fever occurred in Kolkata and along the eastern coastal region in the year 1963-64.^[2] And as of today incidence of dengue fever can be seen all over India with incidence more during the rainy and winter season.

Dengue virus belongs to the family Flaviviridae and there are four serotypes of the dengue viruses (DENV) which are referred to as DENV-1, DENV-2, DENV-3 and DENV-4.^[1,2] Dengue virus is a positive stranded encapsulated RNA virus and is composed of three structural protein genes, which encodes the nucleocapsid or core (C) protein, a membrane associated (M) protein, an enveloped (E) glycoprotein and seven non-structural proteins.^[2] There is a transient cross protection among the four types, which weakens and disappears over the months following infection.^[1]

Dengue fever is typically a self-limited disease, on an average it becomes symptomatic after an incubation period of 8-10 days and the

symptoms usually last for about 2-7 days.^[3] It may be asymptomatic or may present with broad range of clinical manifestations which may include from mild fever to a life threatening shock syndrome.^[1] Accompanying symptoms in patients with dengue may include any of the following: Fever, headache, retro-orbital pain, myalgia, arthralgia, nausea, vomiting, generalised weakness, malaise, sore throat, various hemorrhagic manifestations, etc.^[3] The various hemorrhagic manifestations observed in dengue fever are rash, petechiae, gum bleed, conjunctival suffusion, hematuria, PR bleed, malena, etc; which may be due to decreased platelet count in dengue fever.

Dengue virus has been isolated from polymorphonuclear leukocytes, monocyte/macrophages, dendritic cells and others. It has also been detected in megakaryocyte progenitors and circulating platelets. These findings suggest that dengue virus may induce thrombocytopenia via direct interactions with megakaryocytes and platelets.^[4] Dengue virus has also been shown to reduce circulating platelet counts independent of virus attachment or entry into platelets or their precursors. Thus, two mechanisms are probably involved in dengue-induced thrombocytopenia: impaired thrombopoiesis and peripheral platelet destruction.^[4]

WHO 1997 classification

In 1997, the World Health Organization published a classification scheme describing three categories of symptomatic DENV infection: dengue fever (DF), dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS).^[1]

WHO 2009 classification

In 2009, the World Health Organization introduced a revised classification scheme consisting of the following categories: dengue without warning signs, dengue with warning signs and severe dengue.^[1]

Laboratory testing of dengue virus infection is established directly by detection of viral components in serum or indirectly by serology. Detection of viral nucleic acid or viral antigen has high specificity

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but its drawback is that it is more labor sensitive and costly, whereas

serology has lower specificity but is less costly and easily accessible.[1]

Thrombocytopenia

Thrombocytopenia may be associated with a variety of conditions, with associated risks that may range from life-threatening bleeding or thrombosis to no risk at all. Thrombocytopenia is defined as a platelet count below the lower limit of normal (i.e., < 1,50,00/ μ l).[5] The megakaryocyte is the hematopoietic cell that produces platelets. This relationship was first proved by James Homer Wright in 1906, who demonstrated that circulating platelets and a giant bone marrow cell now known as megakaryocyte shared common tinctorial properties when subjected to a modified Romanowsky stain.[6] Each megakaryocyte produces a total of 1000 to 3000 platelets.[6] Thrombopoietin has a major effect on almost all steps of megakaryocyte differentiation and maturation and is produced by the Liver. There is an inverse relationship between the normal platelet count and the normal mean platelet volume, resulting in a roughly constant circulating platelet mass. The body "defends" the total mass of platelets, not the platelet count. Approximately one-third of the total platelet mass is normally sequestered in an exchangeable splenic pool.[6] Platelets circulate with an average life span of 7–10 days.[7] Thrombocytopenia results from one or more of three processes:[7]

- (1) Decreased bone marrow production;
- (2) Sequestration, usually in an enlarged spleen;
- (3) Increased platelet destruction.

Hemostasis depends on an adequate number of functional platelets, together with an intact coagulation (clotting factor) system.

Degree of Thrombocytopenia[5]

Mild: platelet count of 100,000 to 150,000/ μ l

Moderate: platelet count of 50,000 to <1,00,000/ μ l

Severe: platelet count of <50,000/ μ l

Actively bleeding patients with thrombocytopenia should be transfused with platelets immediately to keep platelet counts above 50,000/ μ l in most bleeding situations including disseminated intravascular coagulation (DIC), and above 1,00,000/ μ l if there is central nervous system bleeding.[8]

Platelets can be transfused therapeutically (i.e., to treat active bleeding or in preparation for an invasive procedure that would cause bleeding), or prophylactically (i.e., to prevent spontaneous bleeding). The threshold for prophylactic transfusion varies depending on the patient and on the clinical scenario; as an example, some patients with ITP often tolerate very low platelet counts without bleeding. "Therapeutic transfusion" refer to both transfusion of platelets to treat active bleeding and transfusion of platelets in preparation for an invasive procedure that could cause bleeding. The term "prophylactic transfusion" is used to refer to platelet

transfusion given to prevent spontaneous bleeding. Prophylactic platelet transfusion is done to prevent spontaneous bleeding in most afebrile patients with platelet counts below 10,000/ μ l due to bone marrow suppression, whereas higher thresholds (i.e., 20,000 to 30,000/ μ l) in patients who are febrile or septic.[8]

Aims and objectives

To study the different bleeding tendencies in dengue fever and its relation with platelet count.

Materials and methods

An observational study was conducted on 150 patients who were diagnosed with Dengue and were admitted in the ward of Department of General medicine, in a Tertiary care hospital, Rohtas, Bihar. All the patients admitted were above the age of 18 years and diagnosed with dengue fever were included in this study. Any patients with known platelet disorders, e.g: ITP, Drug induced, cirrhosis, DIC, etc. were excluded from this study. All the patients admitted underwent basic investigation tests to confirm the diagnosis and complete blood count along with platelet count was done. The patients were observed for presence of any bleeding manifestations such as rash/petechiae, bleeding gums, conjunctival suffusion, epistaxis, hematuria, melena, bleeding per-rectal, etc. All the observations were monitored and recorded along with the platelet count and was statistically analysed.

Results

During this study period, which included 150 patients and were diagnosed with dengue fever was observed who fulfilled the study criteria. In this study a preponderance of males was seen with 95 male patients (63.33%) and the female patients consisted of 55 (36.67%) out of 150 patients. The male female ratio was 1.72:1; as depicted in Table 1 and Fig. 1. Majority of the patients belonged to the age group of 21-30 years (32.67%), followed by 41-50 years (18.67%); 31-40 years (16.67%), less than 20 years contributed to 16% of patients, whereas 51-60 years (11.33%) and least incidence was seen in age group above 61 years (2.67%), which is depicted as in Table 2 and Fig. 2.

The bleeding incidence was seen in only 49 patients out of total 150 patients, which was 32.67% of the study population. There was no evidence of any bleeding sign in 101 patients (67.33%) out of the 150 patients; which is as depicted as in Table 3 and Fig. 3. Study of platelet count values showed that 42 patients (28.0%) showed severe thrombocytopenia, 68 patients (45.33%) patients showed moderate thrombocytopenia and 40 patients (26.67%) showed mild or normal platelet count; as depicted in Table 4 and Fig. 4.

Table 1: Gender Distribution

Gender	No. of Patients (150)	Percentage (%)
Males	95	63.33%
Females	55	36.67%
M : F	1.72:1	

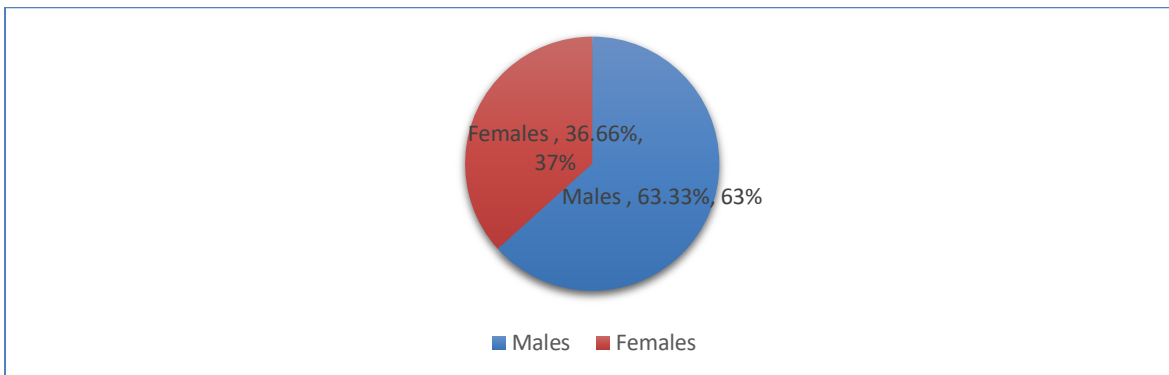


Fig 1: Gender distribution

Table 2: Age distribution

Age	No. of Patients (150)	Percentage (%)
≤20	24	16%
21-30	49	32.67%
31-40	25	16.67%
41-50	28	18.67%
51-60	17	11.33%
>61	4	2.67%

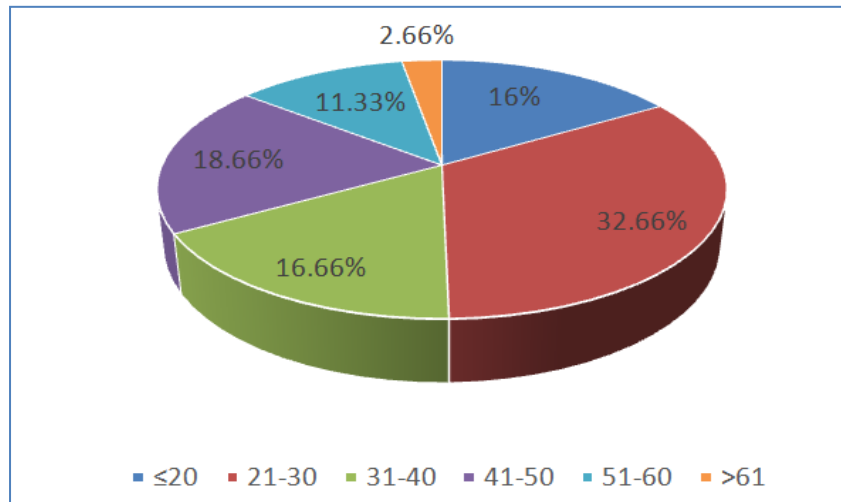


Fig 2: Age distribution

Table 3: Bleeding incidence

	No. of Patients	Percentage
Bleeding manifestations	49	32.67%
No Bleeding manifestations	101	67.33%
Total	150	

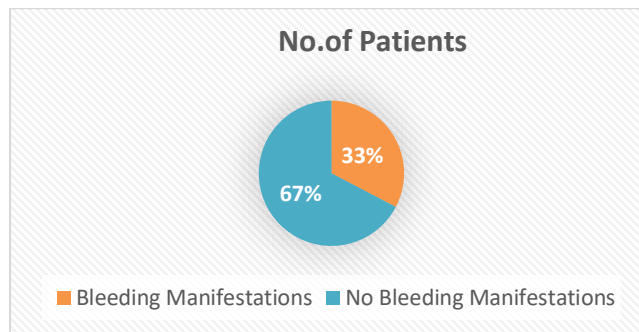


Fig. 3: Bleeding incidence

Table 4: Platelet count

Platelet Count (µl)	No. of Patients (150)	Percentage (%)
≥1 Lakh (MILD)	40	26.67%
50 THOUSAND TO 1 LAKH (MODERATE)	68	45.33%
< 50 THOUSAND (SEVERE)	42	28.0%

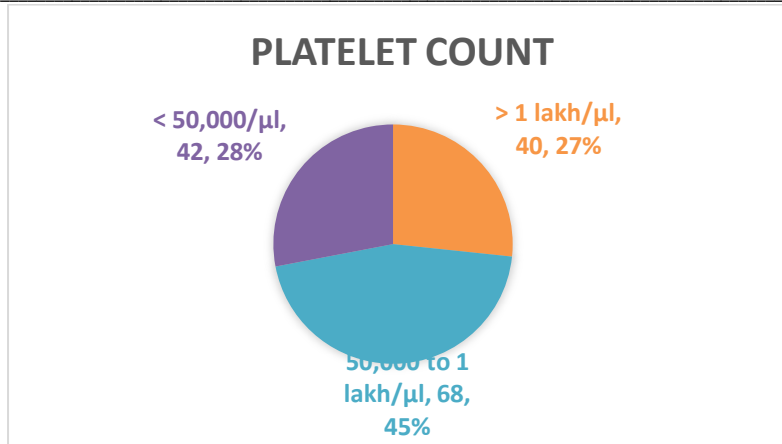


Fig. 4: Platelet count

A total of 49 patients showed bleeding manifestations, which occurred as a single sign or in combination. 48 patients (97.9%) presented with rash/petechiae; 2 patients (4%) presented with hematuria, 4 patients (8.1%) presented with malena, 3 patients (6.1%) presented with PR bleed, 13 patients (26.5%) presented with gum bleed, 10 patients (20.4%) presented with conjunctival suffusion and 6 patients (12.3%) presented with epistaxis. This is depicted in Table 5 and Fig. 5.

Table 5: bleeding tendencies (single or in combination)

Bleeding tendencies	No. of Patients (49)	Percentage (%)
Rash/Petechiae	48	97.9%
Hematuria	2	4%
Malena	4	8.1%
PR Bleed	3	6.1%
Gum Bleed	13	26.5%
Conjunctival suffusion	10	20.4%
Epistaxis	6	12.3%

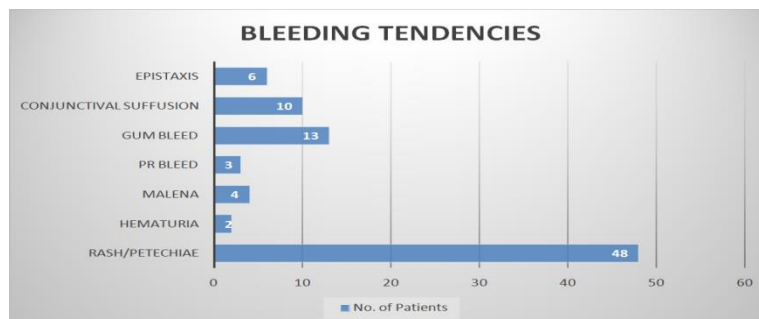


Fig. 5: Bleeding tendencies (Single or in combination)

Bleeding tendencies with relation to platelet count values showed that rash/petechiae was presented in 37 patients (24.7%) with severe thrombocytopenia and 11 patients (7.3%) with moderate thrombocytopenia. Similarly, only 2 patients (1.3%) presented with hematuria in severe thrombocytopenia, 4 patients (2.7%) presented with malena with severe thrombocytopenia. 3 patients (2%) presented with PR bleed in severe thrombocytopenia, 11 patients (7.3%) presented with gum bleed in severe thrombocytopenia and 2 patients (1.3%) in moderate thrombocytopenia. 8 patients (5.3%) presented with conjunctival suffusion in severe thrombocytopenia and 2 patients (1.3%) in moderate thrombocytopenia. 6 patients (4%) presented with epistaxis in severe thrombocytopenia. There was no bleeding manifestations observed in mild thrombocytopenia. This is depicted in Table 6 and Fig. 6.

Table 6: pPlatelet count relation with bleeding tendencies

Bleeding Tendencies	<50,000/μl		50,000/μl to 1 Lakh/μl		> 1 Lakh/μl	
	No. of patients	%	No. of patients	%	No. of patients	%
Rash/Petechiae	37	24.7%	11	7.3%	—	—
Hematuria	2	1.3%	—	—	—	—
Malena	4	2.7%	—	—	—	—
PR Bleed	3	2%	—	—	—	—

Gum Bleed	11	7.3%	2	1.3%	—	—
Conjunctival suffusion	8	5.3%	2	1.3%	—	—
Epistaxis	6	4%	—	—	—	—

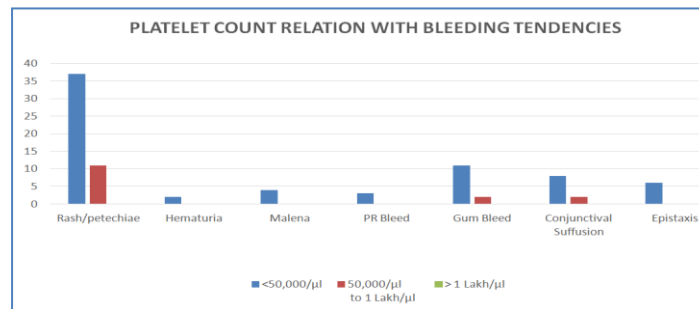


Fig. 6: Platelet count relation with bleeding tendencies

Discussion

Dengue is one of the most common infection occurring during the monsoon and winter seasons. It is also one of the most common causes of fever associated with thrombocytopenia. It is observed to be present with various degrees of thrombocytopenia and may usually present with severe degree of thrombocytopenia (Platelet count < 50,000/μl) which is associated with various bleeding manifestations and which may be indicative for platelet transfusion; either therapeutically or prophylactically. Platelets can be transfused therapeutically (i.e, to treat active bleeding or in preparation for an invasive procedure that would cause bleeding) or prophylactically (i.e, to prevent spontaneous bleeding).[8]

Following platelet transfusion, the platelet count should rise, with a peak at 10 minutes to one hour and with gradual decline over 72 hours. A general rule of thumb is that transfusion of six units of pooled platelets or one apheresis unit should increase the platelet count by approximately 30,000/μl in an adult of average size.[8] There are no substitutes for platelet transfusion to rapidly increase the platelet count in a bleeding patient.[8] Hence, in a patient presenting with bleeding manifestations with low platelet count are advisable for platelet transfusion so as to decrease and prevent the bleeding manifestations, and thus help in decreasing the mortality rate in patients suffering from dengue.

In the study conducted by Radhika B.V. et.al[9] and Jacob K. Jacob[10] where dengue was found to be the major etiological cause of thrombocytopenia in patients who presented with fever, and in our study showed a preponderance of male patients which was in accordance to the study conducted by Radhika B.V. et.al[9] and Jacob K. Jacob[10]

The manifestation was most prominently present in the age group of 21-30 years of age, with most incidence in the age spanning from 18 years to 50 years of age; this was found to be in accordance with the study conducted by Radhika B.V. et.al[9] which had majority of patients (92.5%) belonging to the age group of 18-40 years; whereas in the study conducted by Jacob K. Jacob[10] showed that 40 - 49 year age group was mostly affected (21.95%), followed by 20-29 year age group (21.14%)

In our study we found that the patients mostly presented with moderate level of thrombocytopenia, it was found to be in accordance with the study conducted by Radhika B.V. et.al⁹ and Jacob K. Jacob[10].

In our study 49 out of 150 patients (32.67%) presented with bleeding manifestations. In our study we found that majority of the patients presented with manifestation of skin bleeding in the form of

rash/petechiae, which was similar and in accordance to the study done by Radhika B.V. et.al[9].

Conclusion

Dengue is one of most common cause of febrile infection which mostly present with thrombocytopenia in most of the patients. Thrombocytopenia is one of the major causes for mortality in these patients who develop bleeding manifestations, which serve as a warning sign on clinical examination and also serves the need to evaluate the platelet count at regular intervals and also help in deciding the need for platelet transfusion. Platelet transfusion if done timely in these patients will help in reducing the bleeding manifestations and also keep the platelet count in check. This will help in managing the patients suffering from dengue and also help in reducing the mortality rates.

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