

# LOW PLATELET COUNT ASSOCIATED WITH DENGUE HEMORRHAGIC FEVER

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## Abstract

*Dengue is an infectious mosquito borne disease of tropical regions. There is a drastic change in the demographic characteristics of dengue fever in Pakistan over the past years. Many small studies have been done previously all over the country but the data reported so far regarding demographic, biochemical and hematological parameters of dengue infection is insufficient. This study was undertaken to establish a possible association of decrease in platelet count with bleeding tendency in dengue patients. It is an observational cross-sectional study conducted on 50 sero positive cases during the early days of dengue virus infection (1-7 days) confirmed by Real time PCR (CDC Atlanta) in a tertiary care hospital in Lahore. Patients of both sexes and all age groups were included. The study was approved from ethical committee of King Edward Medical University. 3-5 ml of venous blood was taken from the patients during first 7 days of infection for CBC analysis. Consent was taken from patients or guardian in case of children and proforma was also filled after interviewing the patient. This article assesses the association of severity of disease with age, gender, platelet count and bleeding tendencies in dengue patients. More dengue patients had declined platelet counts (<50,000/ $\mu$ l). Dengue infection was more in age group 16-30 years but hemorrhagic signs were more in females and in older patients. Out of 50 patients 22 were males and 28 were females. Platelet count of dengue patients is mostly less than 150,000 per micro liter while normal range is 150,000 to 400,000 per micro liter. Platelet count of female patients is lower as compared to males, DHF is more in females and Hb has no correlation with bleeding tendency while an association has been found between low platelet count and increased bleeding tendency among the infected patients. Median age of dengue patients has decreased and younger patients especially males may be more susceptible.*

**KEY WORDS:** Dengue, platelet count, bleeding tendency, Lahore

## INTRODUCTION

Dengue epidemic is one of the most important public health problems in the tropical and subtropical regions[1]. Dengue Fever (DF) and Dengue Hemorrhagic Fever (DHF) are caused by a mosquito-borne flavivirus[2]. Dengue virus (DENV) has emerged in the later half of the 20th century to become an important cause of morbidity and mortality. Over half of the world's population lives at risk of infection annually[3]. DF may result from infection with any of the four antigenically related dengue virus serotypes (DEN-1, -2, -3, or -4) [4]. About two-thirds of the world's population lives in areas infested with dengue vectors, mainly *Aedes aegypti*. All four dengue viruses are circulating, sometimes simultaneously, in most of these areas[5].

In Asian countries the disease continues to affect children predominantly although a marked increase in the number of DHF cases in people over 15 years old has been observed in the Philippines and Malaysia during recent years. The clinical manifestations of DF range from a mild, flulike and self-limited febrile illness to severe illness with hemorrhagia. DHF in general and its most severe clinical form, dengue shock

syndrome (DSS), in particular has been one of the major causes of death among children in some Asian countries where DF is endemic[6].

DHF is a severe febrile disease, characterized by abnormalities in hemostasis and increased vascular permeability, which in some cases results in hypovolemic shock syndrome and in dengue shock syndrome. The clinical features of DHF include plasma leakage, bleeding tendency and liver involvement[7].The emergence of dengue throughout the tropical world is affecting an increasing proportion of adult cases.The major pathophysiological hallmark that distinguishes DHF from DF is plasma leakage as a result of increased vascular permeability. Following this leakage, hypovolaemic shock occurs as a consequence of a critical plasma volume loss. Constant haematological abnormalities occurring in DHF and frequently include bone marrow suppression, leucopenia and thrombocytopenia. An enhanced immune response of the host to a secondary DV infection is a feature of DHF and leads to many consequences. These are immune complex formation, complement activation, increased histamine release and a massive release of many cytokines into the circulation, leading to shock, vasculopathy, thrombopathy and Disseminated Intravascular Coagulation (DIC). Thrombopathy consists of thrombocytopenia and platelet dysfunction. DIC is prominent in patients with shock. The most severe DIC and massive bleeding are the result of prolonged shock and cause a fatal outcome [8].

Thrombocytopenia may be occasionally observed in dengue fever (DF) but is a constant feature and one of the diagnostic criteria of DHF[9].DHF and DSS are characterized by plasma leakage resulting from alteration in microvascular permeability[10].Supportive fluid therapy is effective in preventing the onset of shock from excessive plasma leakage but relies on early diagnosis of dengue and monitoring for the clinical signs of plasma leakage[11]. Early diagnosis would have an increasingly important role with the development of antiviral therapies, because the effectiveness of antivirals is likely to be high only if initiated early after illness onset (Tricou 2010), during the short viremic phase[12].

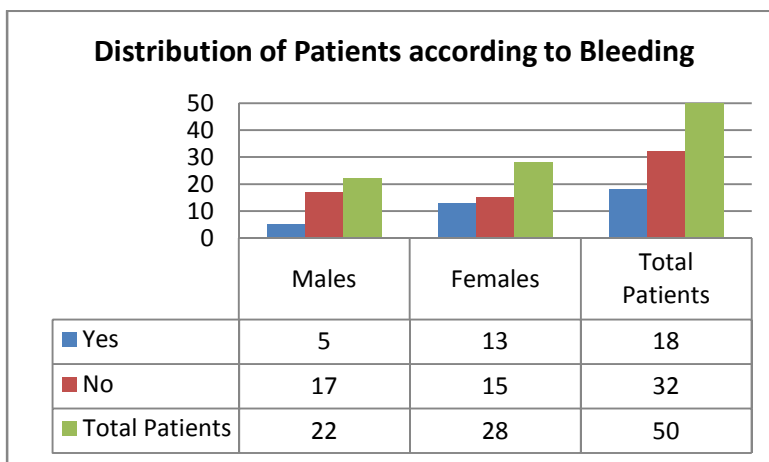
### **Material and Methods:**

According to the proposed study, 3-5ml of venous blood was collected from 50 patients, among which 22 were males and 28 females, within first 7 days of infection, with clinical presentation of Dengue fever (DF) (high grade fever, rash, retro-orbital pain and bleeding) during August-November 2011 (active phase of outbreak), at laboratories of the Pathology Department of King Edward Medical University, Lahore, in collaboration with the Emergency and Accidents Department of Mayo Hospital, Lahore. The samples were collected with proper protocol and consents were taken from the patients or their guardians. All other ethical issues were considered during the process of sampling. Moreover, an approval was taken from the Ethical Consideration board of KEMU. Samples were allowed to clot for half an hour, then samples were centrifuged and serum was separated.Data on sex, age and the presence or absence of bleeding was taken. The inclusion criteria for the study was patients of both sexes and all age groups, with high grade fever, having low platelet count, patients without prior treatment, who were quite healthy before the dengue infection during that outbreak. The samples were sent to the Center of Disease Control (CDC), Atlanta, Georgia, for the purpose of PCR based molecular assays for the determination of the serotypes. All measures were taken for the proper preservation of the samples during their transport to the laboratories of the CDC. Patients were divided into 6 age groups; 1-15, 16-30, 31-45, 46-60, 61-75 and 75 years and above. Data was analyzed by using SPSS version 17.

### **Results and Discussion:**

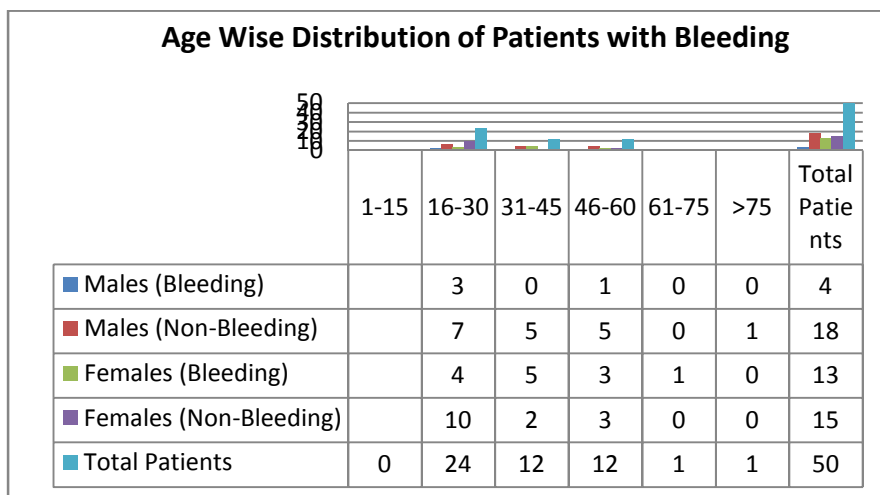
All the dengue positive patients were infected by DEN-2 serotype which was confirmed from CDC Atlanta. Majority of the patients were in the age group of 16-30 years (24/50; 48%), 12 patients (24%) in

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 age group of 31-45 years, 24% in 46-60 years and only 2% in 61-75 years age group and above (Figure 3). There was no patient in the age group of 1-15 years (0%)

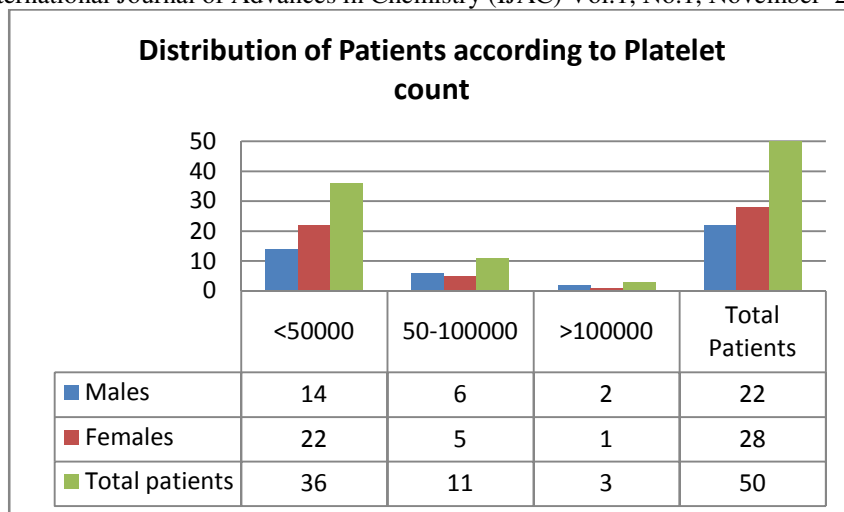


**Figure 1:** Distribution of Patients according to Bleeding

5 (18.2%) male patients out of 22 and 13 (46.5%) female patients out of 28 have bleeding from nasal cavity and in vomit and have dengue hemorrhage fever. 17 (72%) out of 22 male and 15 (53.6%) out of 28 have no bleeding and have simple dengue fever, the present study can conclude that females are more susceptible of dengue hemorrhage fever (Figure 1). Total 22 (70.27%) of these patients were male and mostly didn't show any hemorrhagic signs (Figure 1) and platelet count was less than 50,000/ $\mu$ l in infected patients (Figure 3). There was no association between bleeding tendency and dengue infection (Figure 3). Younger age group 16-30 years was infected more (Figure 2).



**Figure 2:** Age wise distribution of Patients with Bleeding

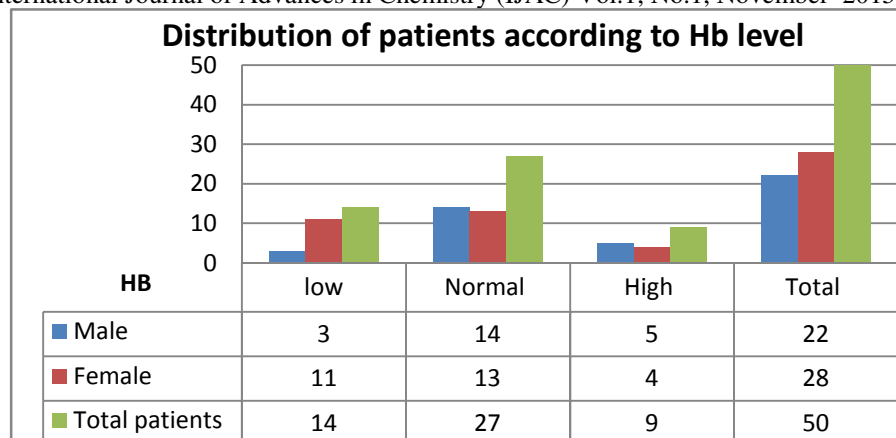


**Figure 3:** Distribution of Patients according to Platelet count

Platelet count is less than 150,000/ $\mu$ lin dengue patients, less than 50,000 platelets per micro litter cause dengue hemorrhagic fever because density of blood become very low causing bleeding, here it can conclude that there is a correlation between platelet count and dengue infection (figure 4, Table 1).

Age Range	Dengue cases						Total		Total cases
	>50000		51000-100000		>100000		M	F	
Plt count	M	F	M	F	M	F	M	F	
1-15	0	0	0	0	0	0	0	0	0
16-30	8	11	02	02	0	01	10	14	24
31-45	03	06	01	01	01	0	05	07	12
46-60	03	04	02	02	01	0	06	06	12
61-75	0	01	0	0	0	0	0	01	01
>75	0	0	01	0	0	0	01	0	01
<b>Total Patients</b>	14	21	06	05	02	01	22	28	50

**Table 1:** Age wise distribution of dengue patients according to platecount count



**Figure 4:** Distribution of patients according to Hb level

Younger age group is more susceptible for the dengue infection (16-30 years) according to present study; other studies also give the similar results (20). There is a correlation between dengue infection/platelet counts and bleeding/platelet count, other studies also indicate same results (21). Platelet count of female dengue patients is lower than males so DHF is more in females because platelet count is inversely proportional to bleeding, as less the platelet count more the bleeding (21). There is no correlation of Haemoglobin with bleeding tendency almost all patients were in normal range of Hb. In DHF blood volume may decrease so Hb may also decrease but there is no direct association between dengue infection and Hb.

## CONCLUSION

An association between dengue virus infection and bleeding tendency is observed in this study which is in accordance with the previous studies. Dengue infected patients mostly had low platelet counts. Younger age group upto 30 years was found to be more susceptible to dengue infection but bleeding tendency was more in females. Hb level in dengue patients was not associated with the severity of the disease and most patients had normal Hb levels.

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