

# Evaluation of Thrombocytopenia and Anemia along with seasonal variations in Dengue Fever

Nadia Kashif<sup>1</sup>, Shama Iqbal<sup>1</sup>, Rashid Ahmad<sup>2</sup>, Afshan Ahsan<sup>3</sup>, Naveed Afzal Khan<sup>3</sup>, Shahid Ali Shah<sup>4</sup>

## Abstract

Dengue fever is arboviral infection that is transmitted through mosquito vector and is among the fastest spreading infection. It has varied clinical presentation of Dengue Fever (DF), Dengue Hemorrhagic fever (DHF), Dengue shock syndrome (DSS) and expended dengue syndrome (EDS) thus creating a diagnostic dilemma. Due to its varied clinical presentation the diagnosis as well as timely management becomes difficult. Anemia and Thrombocytopenia are two of the most important clinical manifestations of dengue patients.

**Objectives:** To evaluate the Frequency and severity of thrombocytopenia in dengue infections.

**Material and Methods:** This cross sectional study was performed in Govt Naseerullah Khan Babar Memorial Hospital Peshawar from April 2019 to October 2019. Blood samples were obtained by non-random convenient sampling from 5000 suspected dengue patients presented with fever and body aches. Serological screening was done and all positive cases were assessed for thrombocytopenia and anemia.

**Results:** Total 826 dengue positive patients were enrolled in this study including 55% males and 45% females. Study results showed 34% patients had thrombocytopenia and 66% patients had normal platelets count. Among total patients 21% were anemic and 79% were non anemic, anemia was more common in females as compared to males patients. Referred to seasonal variations dengue infection was most common in post moon soon period.

**Conclusion:** This cross-sectional study highlighted thrombocytopenia as frequent clinical manifestation of dengue patients that can be life threatening. High temperature, rain and humidity alone or collectively as major contributing factor in dengue infection.

**Key words:** Dengue Infection, Thrombocytopenia, climate

## INTRODUCTION:

Dengue infection is the most prevalent mosquitoes born viral infection worldwide, about 100 million case of dengue fever and half of a million cases of dengue hemorrhagic fever have been reported annually<sup>1, 2</sup>. Dengue infection comprises of acute febrile illness.

Clinical presentation of dengue patients varies but the common symptoms at presentation are fever, myalgia, arthralgia and rash with or without bleeding episodes. In DHF there is hemoconcentration, homeostasis abnormalities and in severe cases patients have fluid and protein loss that leads to DSS.

Dengue fever is arboviral infection that is transmitted through mosquito vector and is among the fastest spreading infection leading to an outbreak in various regions with high temperature, rain and humidity<sup>1, 2</sup>. According to WHO two fifth (2.5) of current population are at risk of dengue fever. In more than 100 countries dengue infection is endemic. Patients suffering from dengue fever are at high risk of developing complications, about one in every 40 patients of dengue die from complication if not treated. Approximately 20 percent of patients having dengue hemorrhagic fever die of infection. Four serotypes of dengue virus has been identified that are different but closely related viruses namely Dengue<sup>1-4</sup>.

Dengue infection is characterized to be seasonal in nature that is common in humid, rainy and hyperthermic environment where it leads to explosive outbreaks<sup>2</sup>. Amusingly the El Nino phenomenon may

---

1. Department of Pathology Govt Naseerullah Khan Babar Memorial Hospital Peshawar, Pakistan.
2. Department of Medicine, Khyber Teaching Hospital, Peshawar, Pakistan
3. Department of Medical Education, Khyber Girls Medical College, Peshawar, Pakistan.
4. Department of Physiology, Khyber College of dentistry, Peshawar.

---

**Corresponding Author:**  
**Dr. Naveed Afzal Khan**

Assistant Director, Medical Education, Khyber Girls Medical College, Peshawar, Pakistan.  
Contact# +923349085561  
Email: [dr.naveed@live.com](mailto:dr.naveed@live.com)

also be associated to the diseases transmitted by mosquitoes that are Malaria and dengue<sup>3</sup>. South Africa, parts of South America and South East Asia are the areas where El Nino cycle has strong impact on climatic conditions.

According to WHO Criteria<sup>3</sup> for diagnosing DHF the following must be present: a) Fever b) hemorrhagic tendency c) thrombocytopenia d) evidence of plasma leakage, manifested by rise in hemetocrit greater than or equal to 20 percent for the age and gender or there should be signs of plasma leakage like asites, pleural effusion and hypoproteinemia. In case of DSS all of the above four signs plus signs of circulatory failure characterized by cold clammy skin, weak pulse, narrow pulse pressure (less than 20mmHg) and hypotension for the age and gender.

Thrombocytopenia in majority of dengue patients is asymptomatic and transient, but in significant number of patients there is bleeding tendency<sup>4</sup>. In patients with platelets count of less than 20,000/cmm spontaneous bleeding has been noted while petichae and purpura is seen in patients with platelets count of 20,000-40,000/cmm. This signifies the importance of assessment of platelets count and the prevalence of DF with thrombocytopenia and follows up after platelets transfusion.

## OBJECTIVES

To evaluate the Frequency and severity of anemia and thrombocytopenia in dengue infections.

## MATERIAL AND METHODS

This cross-sectional study was conducted on indoor and outdoor patients in Naseerullah Babar Memorial Hospital Peshawar from April 2019 –October 2019. All

patients with clinical features of dengue and positive detection of dengue NS1 and Anti dengue IgM antibodies presenting to the hospital during that period were inducted into the study using Non-random convenient sampling.

About 5000 patients suffering from DF were enrolled in this study. All patients presented with fever and body aches were assessed through rapid diagnostic test using combination stripes of NS1, IgM and IgG. The presence of NS1 and Anti dengue IgM antibodies indicates primary infection while presence of anti-dengue IgG antibodies with or without IgM indicated secondary infection. IgG antibodies alone was considered as suspected secondary infection that could be due to cross reactivity with other virus. NS1 and IgM positive cases were processed for complete blood count to assess thrombocytopenia.

The collected data was analyzed using SPSS and simple descriptive statistics were used to interpret the data.

## RESULTS

Total 826 patients were enrolled in this study all patients were dengue NS1, IgM, IgG positive. Data obtained from this study was analyzed for different parameters. Out of total 826 patients 55% were males and 45% were females indicating dengue is more common in male gender.

Patients included in the study were divided in to six age groups based on their ages as shown in table 1. The collected data showed dengue is equally common in age group 2, 3, 4 and 5 and with advancing age frequency of dengue increases in male gender. (Table: 1)

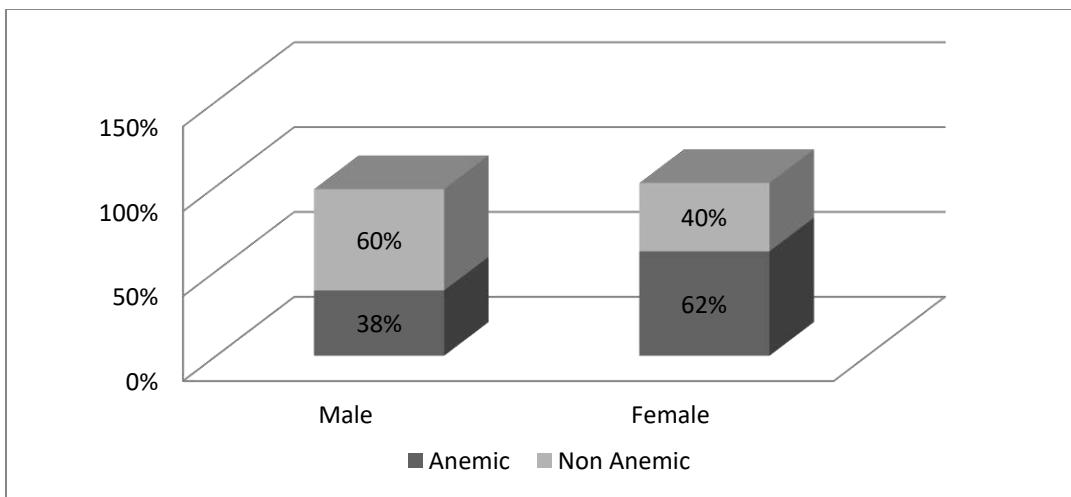
**Table1: Age & Gender wise Dengue Patients**

S.no	Age Groups	Number of Patients	Male Patients	Females Patients
1.	Group 1 (1-15years)	125	81(65%)	44(35%)
2.	Group 2 (16-30years)	393	211(54%)	182(46%)
3.	Group 3 (31-45years)	166	94(57%)	72(43%)
4.	Group 4 (46-60years)	127	61(48%)	66(52%)
5.	Group 5 (61-75years)	9	5(56%)	4(44%)
6.	Group 6 (76-90years)	3	3(100%)	0(0%)

Our study showed that out of 823 patients 21% of patients were anemic and remaining 79% of study patients were non-anemic and thus Anemia was not a common finding in dengue patients.

Data was analyzed to look for the frequency of anemia in both genders of dengue patients. Results

showed that out of total male patients 38% of males were anemic and 60% of males were non anemic, 62% of females were anemic and 40% of females were non anemic. Study results showed that anemia is more common in females suffering from dengue as compared to males. (Figure: 1)



**Figure 1: Gender wise Anemic & Non Anemic Patients**

The collected data showed that out of total 826 patients 34% of patients had thrombocytopenia and 66% of patients were having platelets count in normal

range. The frequency and grading of thrombocytopenia among the male and female patients is showed in table 2.

**Table 2: Grading of Thrombocytopenia with Gender wise distribution**

Thrombocytopenia Grading	Platelet Count	Number of Patients	Male Patients	Females Patients
Grade IV	<25,000	16	7 (44%)	9 (56%)
Grade III	25,000-50,000	15	11 (73%)	4 (27%)
Grade II	50,000-75,000	16	10 (63%)	6 (38%)
Grade I	75,000-150,000	237	138 (58%)	99 (42%)

Thrombocytopenia was more common in male patients as compared to female patients according to study results and grade III thrombocytopenia was most frequent.

Data obtained through this research was divided in to three groups according to seasonal variation, pre-

moon soon (April, May, June), moon soon (July, August) and post moon soon (September, October, November). Table 3 shows that dengue is most frequent in post moon soon period.

**Table: 3 Seasonal variations in Dengue Patients**

Pre Monsoon	Monsoon	Post Monsoon
0%	25%	75%

## DISCUSSION

Dengue is a self-limiting acute viral infection, in which patient can recover or progress to serious life threatening consequences <sup>5</sup>. During acute infection there is activation of fibrinolysis and coagulation pathways <sup>6,7</sup>. Moreover, it also affects progenitor cells

of bone marrow causing hypo cellularity in it <sup>8-10</sup>. In Pakistan in 2012 world worst epidemic of dengue has occurred resulting in about more than 365 deaths <sup>11</sup>.

In the present study about 826 dengue positive cases were enrolled and their hematological profile assessed. There were 55% male and 45% female patients. Jayashree et all also reported prevalence of

dengue infection common in males about 58%. <sup>8</sup>. Majority of the patients fall in age group between 16 to 75 years i.e. group 2,3,4,5 as shown in table 1. The eldest patient was having age 85 years and the youngest was of 4 years. In India the common age group reported for dengue prevalence is from 21- 30 years<sup>12, 13</sup>.

During the early phase of dengue infection it has been suggested by the report of different studies that dengue virus cause attenuation of megakaryocyte and decrease the proliferative ability of haemopoietic cells <sup>14-17</sup>. That leads to abnormality in patient hematological profile. In our study we evaluated prevalence of anemia in these dengue patients. We found out that anemia was present in 21% of patients and about 71% were non-anemic. Study report coincides with the report of Sheekar et all who also find no significant correlation between Dengue and mean hemoglobin level<sup>18</sup>. Moreover, the present study also finds high prevalence of anemia in female 62% in dengue virus infected patient's (Figure: 1). High prevalence of anemia in females can be due to different secondary causes such as malnutrition, pregnancy and chronic illness <sup>19</sup>. As in Pakistan 50% of females have hemoglobin below 11g/dl <sup>20</sup>. However, further research is needed to concentrate on the factors associated with anemia in dengue infection.

Beside anemia we also assessed the effect of dengue on other hematological parameters like platelets. Platelets which are derived from megakaryocyte in bone marrow, have life span of about 8-10 days and are involved in primary homoeostasis forming thrombus at injury site <sup>21-23</sup>. In both shock and non-shock DENV infected patients there is suppression of platelet aggregation there is suppression has been observed <sup>5</sup>. In the current study thrombocytopenia was present in 34% patients table 2. Ahmad S et all reported a high prevalence about 85% <sup>18</sup>. The common pattern of thrombocytopenia was Grade III affecting 73% males and 25% female patients table 2. Khan et al reported presence of mild to moderate thrombocytopenia in 65.2% cases<sup>24</sup>. Study has shown that in mild to moderate thrombocytopenia case there is 23% chances of bleeding <sup>25</sup>. Furthermore, presence of other co morbidities like diabetes or allergies increase 2.5 times the risk of developing complication such DHF, which can cause death <sup>5</sup>.

As currently there is no vaccine available for dengue infection. Thus prevention is the only tool available for its control. The present study assessed the relation

between dengue and seasonal variation. It was observed that 25% cases occurred in monsoon season and 75% in post monsoon respectively (table 3). Our finding are in close conformity with the study report of Pruthvi et all documenting 40.5% cases in post moon soon period <sup>25</sup>. Dengue has been found to be strongly related to temperature and rainfall <sup>10</sup>. A significant increase in mosquito larva has been observed during rainy season <sup>22</sup>. As in post monsoon period there is abundance of rain water reservoir available with optimal temperature and excess humidity in air causing rapid breeding, transmission and propagation of virus. That leads to massive outbreak <sup>25</sup>. It is therefore recommended that different strategies should be designed to prevent this easily controllable life threatening disease.

## CONCLUSION

This cross-sectional study highlighted thrombocytopenia as frequent clinical manifestation of dengue patients that can be life threatening. High temperature, rain and humidity alone or collectively were highlighted as major contributing factor in dengue infection

## DECLARATION

We

- Undersigned author(s) of the submitted manuscript hereby certify that this manuscript is currently not under review by any other journal and will not be submitted to any other journal while it is under review at Life and Science
- Certify that the approval of Institutional Review Board / Institutional Ethics Committee has been included as a statement in the manuscript
- Declare that this manuscript has been checked for plagiarism
- Take full responsibility of the content reported in the manuscript
- Declare that all those who have substantial, direct, intellectual contribution to the conception, design, analysis writing and/or interpretation of data are included as authors.
- Confirm that corresponding author will be responsible for all communication regarding the submitted manuscript

## Author's contribution

S.n o	Author name, Designation	Email/cell number	Contribution
1	Dr Nadia Kashif. District Pathologist NKBM Hospital Peshawar, Pakistan.	Nadia.tila12@gmail.com/03002554197	First author, concept and design of work
2	Dr. Shama Iqbal, Medical officer NKMB Hospital, Peshawar	Rayanafridi1@gmail.com 03329872005	Data Collection
3	Dr. Rashid Ahmad, Senior registrar Medical D ward KTH, Peshawar	dr.rashidahmad570400@gmail.com 03005860585	Data Collection
4	Ms. Afshan Ahsan, Academic Curriculum Coordinator, Khyber Girls Medical College, Peshawar, Pakistan	Mountainfly87@hotmail.com 03339928187	Data Analysis and interpretation
5	Dr. Naveed Afzal khan, Assistant Director Medical Education, Khyber Girls Medical College, Peshawar, Pakistan	dr.naveed@live.com 03349085561	Drafting manuscript, Review and corresponding author
6	Dr. Shahid Ali Shah, Assistant Professor Physiology. Khyber college of dentistry, Peshawar.	dr.s.a.shah@live.com 03335044097	Data Collection

## Conflict of interest

The authors whose names are listed above certify that they have no affiliations with or involvement in any organization or entity with any financial interest.

## Funding

No outside source of funding was used. The study and publication is by the personal expense of the authors

## Acknowledgement

We are thankful to Dr Mohammad Siraj MS Naseerullah khan Babar Memorial hospital for allowing us to conduct research in this hospital.

## REFERENCES

- 1) Gibbons RV. Vaughn DW. Dengue an escalating problem BMJ.2001;32(4): 1563-6. doi:10.1136/bmj.324.7353.1563
- 2) Gubler DJ. Epidemic dengue/dengue hemorrhagic fever as a public health social and economic problem in the 21<sup>st</sup> century. Trends in Microbiology.2002;10(2):100-03 doi:10.1016/S0966-842X(01)02288-0
- 3) Dengue Hemorrhagic fever Diagnosis, treatment, prevention and control. Geneva:World Health Organization(2nd edn)
- 4) McGraw Hill. Handian RI. Bleeding and thrombosis. Harrison principles of internal medicine.2001 : ( 15<sup>TH</sup> edn).USA.
- 5) Azeredo D.E.L, et al. Thrombocytopenia in Dengue: Interrelationship between Virus and the Imbalance between Coagulation and Fibrinolysis and Inflammatory Mediators. *Mediat Inflamm* 2015; 313842; 1-16. Doi:10.1155/2015/313842.
- 6) Sosothikul, P. Seksarn, S. Pongsewalak, U. Thisyakorn and J. Lusher, "Activation of endothelial cells, coagulation and fibrinolysis in children with Dengue virus infection," *Thromb Haemost.* 2007; 97(4): 627-634.
- 7) Willis B, et al. Haemostatic changes in Vietnamese children with mild dengue correlate with the severity of vascular leakage rather than bleeding," *Am. J. Trop. Med. Hyg* 2009; 81(4); 638-644, 2009. doi:10.4269/ajtmh.2009.08-0008
- 8) Willis B.A, et al. Coagulation abnormalities in dengue hemorrhagic fever : serial investigation in 167 Vietnamese children with Dengue Shock Syndrome. *Clin. Infect. Dis* 2002; 35: 277-285.
- 9) Orsi, R. N. Angerami, B. M. Mazetto et al., "Reduced thrombin formation and excessive fibrinolysis are associated with bleeding complications in patients with dengue fever: A case-control study comparing dengue fever patients with and without bleeding manifestations," *BMC Infect. Dis* 2013; 13(1):3445- 350.
- 10) S. Green, D. W. Vaughn, S. Kalayanarooj et al., "Early immune activation in acute dengue illness is related to development of plasma leakage and disease severity," *J. Infect Dis* 1999; 179(4): 755-762. Doi:10.1086/314680
- 11) Shakoor MT, Ayub S, Ayub Z . Dengue fever: Pakistan's worst nightmare. *WHO South-East Asia J. Public Health* 2012; 229: 231-229
- 12) Jayashree K, Manasa G.C, Pallavi P, Manjunath G.V. Evaluation of Platelets as Predictive Parameters in Dengue Fever *Indian J Hematol Blood Transfus* 2011; 27(3):127-130 doi:10.1007/s12288-011-0075-1
- 13) Shekar EC et al. A prospective study to analyze the clinical, biochemical and hematological parameters of dengue fever in Mahatma Gandhi

Memorial Hospital, Warangal, Telangana, India. Int J Adv Med.2017 Feb;4(1):218-224  
<http://www.ijmedicine.com> pISSN 2349-3925 | eISSN 2349-3933 ]

- 14) Choudhury B.P. Prevalence and severity of thrombocytopenia in dengue patients. Global. J. Res. Anal 2018: 7(1);2277- 8160.
- 15) Srichaikul T, Nimmannitya S. "Hematology in dengue and dengue hemorrhagic fever," Bailliere's Best .Pract. Res. Clin. Hematol .2000;13( 2); 261-27.
- 16) Shah F, et al. Frequency of Anemia in patients presenting to tertiary care hospital Peshawar, Pakistan. K.M.U.J. 2015; 7(1): 29- 30.
- 17) WHO. The global prevalence of anemia in 2011. GEneva: World Health Organization.2015.
- 18) Coller B.S, Shattil S.J.The GPIIb/IIIa (integrin alphallbbeta3) odyssey: a technology-driven saga of a receptor with A twists, turns and even a bend," Blood 2008: 112 (8); 3011–3025.
- 19) Gawaz, M. H. Langer, May A.E. Platelets Inflammation and atherogenesis," J. Clin. Invest .2005: 115(12); 3378–3384.
- 20) Kaushansky. "Lineage-specific hematopoietic growth factors," New. Eng.J. Med .2006; 354(19):2034–2045.
- 21) Semple W.J, "Recent progress in understanding the pathogenesis of immune thrombocytopenia," Curr Opin in Hematol.2010: vol. 17 (6): 590–595.
- 22) Ahmed S. Dengue fever outbreak: a clinical management experience. J. COLL Physician. Surg. Pak .2008: 18 (1); 8-12 9
- 23) Khan et al. Incidence of thrombocytopenia in seropositive dengue Patients. Int. J. Med. Med. Sci. 2014: 6(4);113-116. DOI: 10.5897/IJMMS2013.1026 ISSN 2006-9723 doi:10.5897/IJMMS2013.1026
- 24) Narayanan M, Aravind MA, Ambikapathy P, Prema R, Jeyapaul MP. Dengue Fever – Clinical and Laboratory Parameters Associated with Complications. Dengue Bull.2003: 27:108-115
- 25) Pruthvi D, et al., Evaluation of Platelet Count in Dengue Fever Along with Seasonal Variation of Dengue Infection. J Blood Disorders Transf. 2012: 3:128. doi:10.4172/2155-9864.1000128