

ORIGINAL ARTICLE

Hematological Indicators Assessing Severity in Dengue PatientsANSA KULSOOM REHMAN¹, HUMAIRA TAJ NIAZI², LAILA BAHADUR³, SABA KHAN⁴, MEHREEN FAROOQ⁵, ASFANDYAR SHAH ROGHANI⁶¹Assistant Professor (Haematology), Kabir Medical College/MMC-General Hospital Peshawar²Assistant Professor (Haematology), Rehman Medical Institute, Peshawar.³Mphil, FCPS Haematology⁴Experiential Registrar Pathology, Peshawar Institute of Cardiology⁵FCPS Haematology, Quality Assurance manager, Regional blood center Peshawar⁶District Pathologist Women and Children hospital Rajjar CharsadaCorresponding author: Asfandiyar Shah Roghani, Email: asfandroghani@gmail.com**ABSTRACT****Background:** Dengue is viral disease of human transmitted by *Aedes aegypti* mosquito. The clinical signs and symptoms of dengue infection range significantly, from mild dengue fever to a severe illness.**Objective:** Our study aims to describe the potential predictive hematological parameters which are associated with severity in dengue patients.**Methodology:** This study was descriptive study conducted at the department of Pathology (Hematology), Maqsood Medical Complex and General Hospital, Peshawar, for duration of six months from 1st May 2022 to 31st October 2022. Blood samples were taken aseptically from all the included patients and were sent to the hospital diagnostic laboratory where the hematological parameters were determined. All the data was collected in a pre-designed proforma. The data analysis was done by using IBM SPSS version 23.**Results:** In the current study, a total of 160 patients were enrolled. There were 102 (63.75%) male patients while female patients were 56 (36.25%). Based on the hematological parameters, the mean (\pm SD) Hematocrit (%), Hemoglobin (g/dl), White cell count (μ L), Lymphocytes(μ L), Neutrophils (%) and Platelets (μ L) in non severe dengue cases vs severe dengue cases were 39.2 (\pm 5.1)% vs 42.3 (\pm 4.3)%, 12.5 (\pm 0.9) g/dl vs 13.9 (\pm 1.8) g/dl, 3290 (\pm 1.4) μ L vs 4750 (\pm 1.6) μ L, 40.6 (\pm 12.19) μ L vs 46.1 (\pm 9.96) μ L, 44.4 (\pm 16.56)% vs 49.4 (\pm 12.44) % and 10,5000 (\pm 1.12) μ L vs 56,000 (\pm 2.36) μ L respectively.**Conclusion:** Our study concludes that some common hematological markers have a substantial correlation with the severity of dengue illness.**Keywords:** Hematological indicators; severe dengue; Non-severe dengue**INTRODUCTION**

Dengue is viral disease of human transmitted by mosquito. DEN1 to DEN4 are the four serotypes of dengue virus. This RNA virus is transmitted by the mosquitoes called *Aedes aegypti* ^{1, 2}. Temperature is considered as the most significant climatic component and has a significant impact on the survival of the dengue virus, among other environmental variables like climate and weather. Dengue fever is a febrile sickness that may manifest in a wide range of clinical presentations, from a few mild symptoms to a severe illness that causes bleeding, shock, and even death ^{3, 4}.

In Pakistan, the dengue virus has been the source of several epidemics. Dengue fever was first identified in Pakistan in 1982, when 12 out of 174 individuals were infected ⁵. Dengue infection may spread from one location to another via travelers. The first reported case of dengue infection was documented in SWAT, in Khyber Pakhtunkhwa in August 2013. In Karachi, the first case of dengue infection was reported in 1994. Data from 2013 show that 3177 cases of dengue fever were reported, placing Khyber Pakhtunkhwa at the top of the list ⁶. A total of 5569 dengue patients, including 37 fatal cases, were hospitalized in Swat between August 2013 and November 2016 ⁷. People between the ages of 16 and 30 made up the majority of dengue cases victims from 2013 to 2015, followed by people between the ages of 31 and 45. The infection rate in males was also twice that of females ⁸. According to the study done by Suleman et al. in 2017, this epidemic illness first spread from Swat to the neighbouring districts of Malakand, Mansehra, lower and upper Dir, Kohat and Peshawar subsequently to other regions including Swabi, Mardan and Nowshera ⁸.

The clinical signs and symptoms of dengue infection range significantly, from mild dengue fever to a severe illness known as dengue shock syndrome that is marked by severe plasma leakage and bleeding manifestations. Several parameters for clinical and laboratory diagnosis of dengue are recommended by the World Health Organization (WHO) to aid doctors in making a diagnosis and identifying the categorization of dengue infection ⁹.

Prolonged shock, extensive bleeding, and fluid overload are the main causes of death from dengue illness. The main issue that

results in a poor prognosis or mortality when patients arrive to hospitals in severe situations is that they are not diagnosed ^{10, 11}. Studies have been done on clinical risks and laboratory testing to predict the severity of infection.

The most noticeable haematological alteration is leukopenia, however lymphocytosis—the presence of aberrant lymphocytes—is also often seen. DHF is characterised by thrombocytopenia with elevated hematocrit levels. The provision of particular treatment that assures a significant decrease in the rate of the illness itself depends on the early identification of dengue.

It is crucial to stratify these individuals and identify those who need immediate attention since between 2% and 5% of patients with dengue infection has serious consequences. This is essential in nations where resources are few in order to lessen the burden placed on the health care system ¹². Our study aims to describe the potential predictive hematological parameters which are associated with severity in dengue patients.

MATERIALS AND METHODS

This study was descriptive study conducted at the department of Pathology (Hematology), Maqsood Medical Complex and General Hospital, Peshawar. The study duration was six months from 1st May 2022 to 31st October 2022. The sample size was 160 based on WHO sample size calculator. Non-probability sampling technique was used. All the patients of both the genders and all ages, diagnosed with dengue virus infection on Dengue NS1 (ICT) were included. All the patients with blood disorders, malignancy, immune system related problem and patients not willing to participate in our study were excluded. After ethical approval, the study was explained in detail to all the participants and then written informed consent was taken. Blood samples were taken aseptically from all the included patients and was sent to the hospital diagnostic laboratory where the hematological parameters like Hematocrit (%), Hemoglobin (g/dl), White cell count (μ L), Lymphocytes(μ L), Neutrophils (%) and Platelet (μ L) were determined. All the data was collected in a pre-designed proforma. The data analysis was done by using IBM SPSS version 23. Means and standard deviations were determined for qualitative

variables like age and hematological parameters whereas frequencies and percentages were determined for quantitative variables like gender. For statistical significance chi-square test was employed.

RESULTS

In the current study, a total of 160 patients were enrolled. There were 102 (63.75%) male patients while female patients were 58 (36.25%). (Figure 1) Based on age distribution, 65 (40.63%) patients were less than 20 years, 45 (28.13%) patients were in range of 21-40 years, 38 (23.75%) patients were in age range 41-60 years while only 12 (7.27%) patients were in age group 61-80 years. (Figure 2) Based on disease severity, 104 (65%) patients were observed with non-severe dengue while 55 (35%) patients were observed with severe dengue. (Figure 3) Based on the hematological parameters, the mean (±SD) Hematocrit (%), Hemoglobin (g/dl), White cell count (/ μ L), Lymphocytes(/ μ L), Neutrophils (%) and Platelet (/ μ L) in non severe dengue cases were 39.2 (±5.1)%, 12.5 (±0.9) g/dl, 3290 (±1.4) / μ L, 40.6 (±12.19)/ μ L, 44.4 (±16.56) %, 105000 (±1.12) / μ L respectively while the mean (±SD) Hematocrit (%), Hemoglobin (g/dl), White cell count (/ μ L), Lymphocytes(/ μ L), Neutrophils (%) and Platelet (/ μ L) in severe dengue cases were 42.3 (±4.3)%, 13.9 (±1.8) g/dl, 4750 (±1.6) / μ L, 46.1 (±9.96) / μ L, 49.4 (±12.44) %, 56000 (±2.36) / μ L respectively. (Table 1)

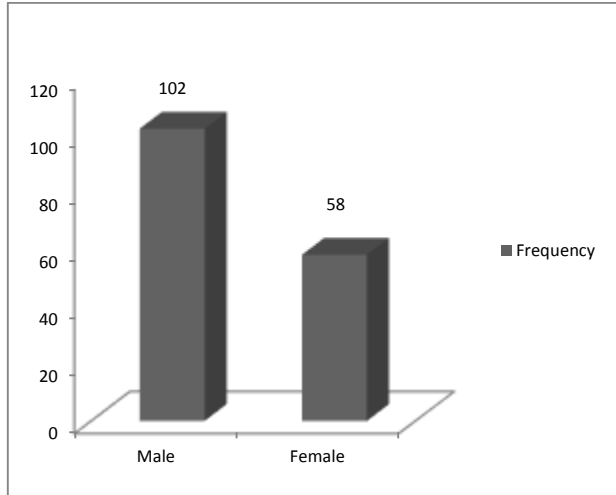


Figure 1: Distribution of patients based on gender

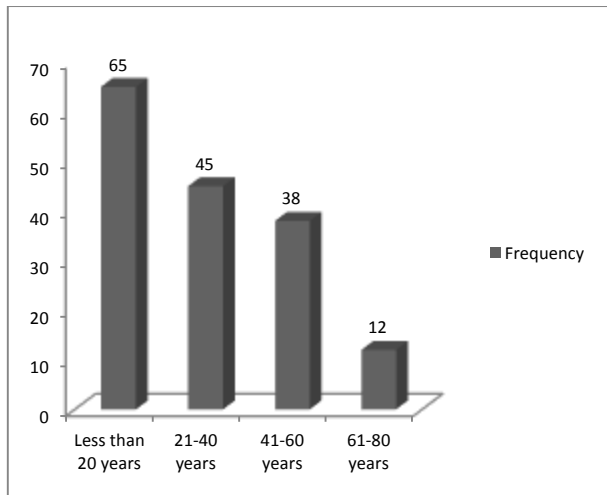


Figure 2: Distribution of patients based on age

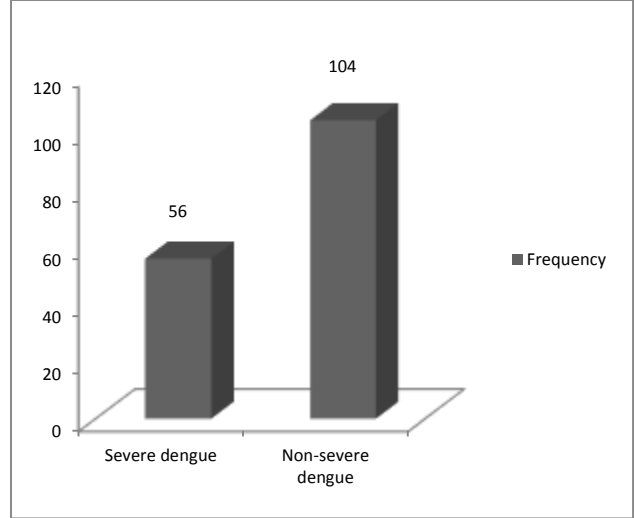


Figure 3: Distribution of patients based on disease severity

Table 1: Comparison of hematological parameters in severe and non severe dengue

Hematological parameter	Disease severity	Mean (±SD)	P value
Hematocrit (%)	Non severe dengue	39.2 (±5.1)	0.001
	Severe dengue	42.3 (±4.3)%	
Hemoglobin (g/dl)	Non severe dengue	12.5 (±0.9)	0.276
	Severe dengue	13.9 (±1.8)	
White cell count (/ μ L)	Non severe dengue	3290 (±1.4)	0.001
	Severe dengue	4750 (±1.6)	
Lymphocytes(/ μ L)	Non severe dengue	40.6 (±12.19)	0.419
	Severe dengue	46.1 (±9.96)	
Neutrophils (%)	Non severe dengue	44.4 (±16.56)	0.001
	Severe dengue	49.4 (±12.44)	
Platelet (/ μ L)	Non severe dengue	105000 (±1.12)	0.001
	Severe dengue	56000 (±2.36)	

DISCUSSION

Especially in tropical and subtropical countries, dengue fever is a critical public health problem that significantly increases morbidity and death in the general population¹³. The symptoms of dengue fever may vary from a low fever to severe organ failure and bleeding. Infection with dengue fever, which is spread by mosquitoes, is widespread in countries like India and Pakistan owing to the country's tropical environment, rapid urbanization, substandard living conditions, and ineffective management of waste disposal. In the current study, hematological parameters were assessed in both severe and non severe dengue infection patients.

In the current study, a total of 160 patients were enrolled. There were 63.75% male patients while female patients were 26.25%. In accordance with our study, a previous study reported more males with dengue infection as compared to females¹⁴. Another study also reported consistent results with our study and reported more males (52%) with dengue infection than females (48%)¹⁵. This could have something to do with the fact that males are more likely to be exposed to mosquito bites because of their jobs and recreational hobbies.

Based on age distribution, 40.63% patients were less than 20 years, 28.13% patients were in range of 21-40 years, 23.75% patients were in age range 41-60 years while only 7.27% patients were in age group 61-80 years in our study. A previous study carried out by Deshwal et al. reported consistent results with our findings and reported that majority of the patients (70%) were <40 years¹⁶. Another study also reported comparable findings¹⁷.

Based on disease severity, 65% patients were observed with non-severe dengue while 35% patients were observed with severe dengue in our research work. Consistent results were reported by

another study. In which they reported that majority (70%) of their study cases were non-severe dengue cases as compared to severe dengue cases (30%)¹⁵. Other studies reported severe dengue cases in the range of 30-40% cases^{18,19}.

Based on the hematological parameters, the mean (\pm SD) Hematocrit (%), Hemoglobin (g/dl), White cell count (μ L), Lymphocytes(μ L), Neutrophils (%) and Platelet (μ L) in non severe dengue cases were 39.2 (\pm 5.1)%, 12.5 (\pm 0.9) g/dl, 3290 (\pm 1.4) μ L, 40.6 (\pm 12.19) μ L, 44.4 (\pm 16.56) %, 105000 (\pm 1.12) μ L respectively while the mean (\pm SD) Hematocrit (%), Hemoglobin (g/dl), White cell count (μ L), Lymphocytes(μ L), Neutrophils (%) and Platelet (μ L) in severe dengue cases were 42.3 (\pm 4.3)%, 13.9 (\pm 1.8) g/dl, 4750 (\pm 1.6) μ L, 46.1 (\pm 9.96) μ L, 49.4 (\pm 12.44) %, 56000 (\pm 2.36) μ L respectively. In accordance with our study, another study reported comparable results²⁰.

Numerous studies have shown that a hematocrit of 40% or higher is a predictor of a more severe dengue infection, especially when assessing DSS²¹⁻²³. Vasculopathy, which is caused by a dengue infection, leads to increased vascular permeability, which in turn induces hemoconcentration and shock^{24,25}. The WHO uses hemo-concentration as one of its diagnostic criteria for DHF. Few studies reported finding no such connection²⁶. Platelets less than 100,000/L increased the probability of severity, which is consistent with numerous studies²¹⁻²³. Before patients went into shock, platelet counts dropped dramatically. The WHO classified dengue infections into DHF grades I to IV using platelets as well. Low platelet count was attributed to bone marrow suppression as well as liver and spleen-induced platelet destruction brought on by immunological response¹⁰. White cell count > 5,000/L was identified in some studies to be a predictive factor for the severity of dengue²⁷, but leucopenia was observed in others^{22,26}. Early dengue infection might cause moderate normoleukocytosis or leukocytosis. The majority of individuals developed leucopenia as a result of bone marrow suppression when their body temperature dropped²⁴.

CONCLUSION

Our study concludes that some common hematological markers have a substantial correlation with the severity of dengue illness. The severity of a dengue infection may be predicted and managed in the future using these factors early in the course of the disease.

REFERENCES

- Munir MA, Alam SE, Khan ZU, Saeed Q, Arif A, Iqbal R, et al. Dengue fever in patients admitted in tertiary care hospitals in Pakistan. *JPMA*. 2014;64(553).
- Khanani RM, Arif A, Shaikh R. Dengue in Pakistan: Journey from a disease free to a hyper endemic nation. *Journal of the Dow University of Health Sciences (JDUHS)*. 2011;5(3):81-4.
- Ebi KL, Nealon J. Dengue in a changing climate. *Environ Res*. 2016;151:115-23.
- Rocha LAd, Tauil PL. Dengue em criança: aspectos clínicos e epidemiológicos, Manaus, Estado do Amazonas, no período de 2006 e 2007. *Rev Soc Bras Med Trop*. 2009;42:18-22.
- Atif M, Raheel U, Alam F, Arshad H, BALOCH F, IMRAN M, et al. Serotyping of dengue virus from deadly outbreaks of Pakistan. *Journal of Human Virology & Retro-virology*. 2016;3(3):00092.
- Haider N, Iqbal A. Dengue prevalence and diagnosis in Pakistan. *International Journal of TROPICAL DISEASE & Health*. 2016;19(2):1-14.
- Khan W, Khan BA, Khan Z, ur Rehman A, Akbar M, Khan IA. DENGUE FEVER: THE CLINICAL PATTERN AND MORTALITY IN EPIDEMIC AND POST EPIDEMIC YEARS IN SWAT. *The Professional Medical Journal*. 2017;24(10):1466-70.
- Suleman M, Faryal R, Alam M, Sharif S, Shaukat S, Khurshid A, et al. Identification of concurrent infection by multiple dengue virus serotypes during an epidemic in 2011 in Pakistan. *Journal Microbiology & Experimentation*. 2016;3(3):00088.
- Organization WH. Comprehensive guideline for prevention and control of dengue and dengue haemorrhagic fever. 2011.
- CHUANSUMRIT A, TANGNARARATCHAKIT K. Pathophysiology and management of dengue hemorrhagic fever. *Transfus Altern Transfus Med*. 2006;8:3-11.
- Buranakitjaroen P. Hypertension audit in clinical practice based in Thailand (HABIT). *J Med Assoc Thai*. 2011;94(2):57.
- Jaenisch T, Tam DTH, Kieu NTT, Van Ngoc T, Nam NT, Van Kinh N, et al. Clinical evaluation of dengue and identification of risk factors for severe disease: protocol for a multicentre study in 8 countries. *BMC Infect Dis*. 2016;16(1):1-11.
- Sharma SK, Seth T, Mishra P, Gupta N, Agrawal N, Broor S, et al. Clinical profile of dengue infection in patients with hematological diseases. *Mediterr J Hematol Infect Dis*. 2011;3(1).
- Vasundhara K, Lavanya A, Rajeswari BV. Clinico-Hematological Parameters in Dengue Fever: A Retrospective Study in a Tertiary Care Hospital. *Age (in years)*.20(9):9.2.
- Mulyaningrum U, Wardani K. Clinical and Hematological Parameters as the Predictors of Shock in Dengue Infection. *Glob Med Heal Commun*. 2018;6:176-81.
- Deshwal R, Qureshi MI, Singh R. Clinical and laboratory profile of dengue fever. *J Assoc Physicians India*. 2015;63(12):30-2.
- Srisuphanunt M, Puttaruk P, Kooltheat N, Katzenmeier G, Wilairatana P. Prognostic Indicators for the Early Prediction of Severe Dengue Infection: A Retrospective Study in a University Hospital in Thailand. *Tropical medicine and infectious disease*. 2022;7(8):162.
- Raihan R, Hadinegoro SRS, Tumbelaka AR. Faktor prognosis terjadinya syok pada demam berdarah dengue. *Sari Pediatri*. 2016;12(1):47-52.
- Yulianto A, Laksono IS, Juffrie M. Faktor prognosis derajat keparahan infeksi dengue. *Sari Pediatri*. 2016;18(3):198-203.
- Pongpan S, Wisitwong A, Tawichasri C, Patumanond J. Prognostic indicators for dengue infection severity. *International Journal of Clinical Pediatrics*. 2013;2(1):12-8.
- Pham T, Nguyen T, Vu T, Nguyen T, Malvy D. Predictive factors of dengue shock syndrome at the children Hospital No. 1, Ho-chi-Minh City, Vietnam. *Bulletin de la Societe de Pathologie Exotique* (1990). 2007;100(1):43-7.
- Chacko B, Subramanian G. Clinical, laboratory and radiological parameters in children with dengue fever and predictive factors for dengue shock syndrome. *J Trop Pediatr*. 2008;54(2):137-40.
- Shah G, Islam S, Das B. Clinical and laboratory profile of dengue infection in children. *Kathmandu Univ Med J (KUMJ)*. 2006;4(1):40-3.
- Srichaikul T, Nimmannitya S. Haematology in dengue and dengue haemorrhagic fever. *Best Practice & Research Clinical Haematology*. 2000;13(2):261-76.
- Lei H-Y, Yeh T-M, Liu H-S, Lin Y-S, Chen S-H, Liu C-C. Immunopathogenesis of dengue virus infection. *J Biomed Sci*. 2001;8(5):377-88.
- Gupta V, Yadav TP, Pandey RM, Singh A, Gupta M, Kanaujia P, et al. Risk factors of dengue shock syndrome in children. *J Trop Pediatr*. 2011;57(6):451-6.
- Azin FRFG, Gonçalves RP, Pitombeira Mhds, Lima DM, Castelo Branco I. Dengue: profile of hematological and biochemical dynamics. *Revista brasileira de hematologia e hemoterapia*. 2012;34:36-41.