

# An Evaluation of Haematological Changes in Paediatric Dengue Fever Patients at a Tertiary Care Hospital Rawalpindi during 2019 Outbreak

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<sup>1,2,3,4</sup> Conception of study

<sup>1,2,3,4</sup> Experimentation/Study conduction

<sup>1,2,3,4</sup> Analysis/Interpretation/Discussion

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## Abstract

**Objective:** The study aimed to evaluate the hematological parameters of patients with dengue fever in order to increase the sensitivity of screening for early diagnosis and as an aid to the early institution of appropriate treatment.

**Materials and Methods:** This study was conducted in Paediatrics Department Benazir Bhutto Hospital, Rawalpindi for a period of 6 months from July 2019 to December 2019.

**Results:** During the study period of 6 months, 438 dengue serology-positive children were admitted, amongst which 254 were male (58%), and 184 were female (42%). The children's age ranged from 1 month to 12 years, with a mean age of 8.03 years (SD  $\pm$  3.13 years). Out of 438 children, 254 (58%) were uncomplicated dengue fever (DF), 119 children (27%) developed dengue hemorrhagic fever (DHF). 65 children (15%) went into dengue shock syndrome (DSS). The predominant findings in the complete blood picture (CBC) were Thrombocytopenia (80.1%) and leucopenia (65.1%). Normal leucocyte count was seen in 59 cases (13.68%). Thrombocytopenia (platelets less than 100,000) was seen in 351 patients (80.1%) out of which 30 cases (6.9%) had a platelet count less than 50,000. Leukopenia was found in 285 (65.1%) patients. Most of the patients were positive for NS1 (70.3%). IgM was positive in 62.1% and IgG was positive in 14.8%. Enteric Fever as co-infection was found in 30(6.8%) children.

**Conclusion:** Careful assessment and interpretation of hematological changes in dengue patients allow early diagnosis and institution of appropriate treatment.

**Keywords:** Dengue, platelets, children.

## Introduction

Dengue is a public health concern as it is a global life-threatening infection. In more than 100 countries it affects about 2.5 billion people.<sup>1</sup>

Dengue is transmitted by mosquitos and leads to arthropod-born viral diseases.<sup>2</sup> Dengue virus is a member of the Flaviviridae family and has four different antigenic types (dengue 1, 2, 3 & 4). The principal vector is *Aedes aegypti* which bites during the daytime.<sup>3</sup>

The main presenting features are fever, headache, myalgia, arthralgia, and minor haemorrhagic manifestations.<sup>4</sup> A wide range of manifestations can occur in infection with any of the dengue virus infections and vary from mild fever to haemorrhage and shock which is life-threatening.<sup>5</sup>

Correct and early diagnosis can help improve patient management and optimized the use of resources such as hospital staff, beds, and equipment.<sup>6</sup>

The laboratory test for dengue is of two types, Non-specific tests like complete blood count and definitive tests like dengue serology and NS1 antigen test.<sup>7</sup> The epidemiological aspects of the disease, the kit, and the method used may result in variations in these tests results.<sup>8</sup>

During the disease process, a series of haematological and biochemical changes occur which depend upon the clinical disease.<sup>9</sup>

The clinical features of dengue infection may resemble other infections. The serological tests are expensive and are not available in many hospitals.<sup>10</sup> Awareness of clinical features, as well as laboratory findings like haematological and biochemical parameters, are the most important guides to therapy and prognosis of dengue fever. The haematological and biochemical findings reported are thrombocytopenia, anemia, leukopenia, elevated levels of AST & ALT.<sup>11</sup> Other findings are activated lymphocytes on a peripheral blood smear.<sup>12</sup> Lymphocytosis and neutrophilia and raised bilirubin can also occur.<sup>13</sup> Changes in haematocrit, albumin, and cholesterol can also occur.<sup>9</sup> Other changes are hemoconcentration<sup>12</sup>, a raised blood urea and serum creatinine<sup>14</sup>, hypokalemia, DIC<sup>15</sup> hypocalcemia.<sup>16</sup> The study aimed to evaluate the hematological parameters of patients with dengue fever to increase the sensitivity of screening for early diagnosis and as an aid to the early institution of appropriate treatment.

## Materials and Methods

This prospective descriptive study was conducted at the Department of Pediatrics, Benazir Bhutto Hospital, Rawalpindi for a period of 6 months from July to December 2019. One month to 12 years old children presenting with clinical signs and symptoms of dengue fever were admitted to the paediatric dengue ward and were included in the study. Patients with age more than 12 years or suffering from previously known blood disorders were excluded. All children attending the hospital with symptoms and signs suggestive of dengue fever were tested for NS1 antigen and IgM/IgG dengue antibody serology (depending on the day of fever) by enzyme-linked immunosorbent assay (ELISA) technique. Every admitted case with confirmed dengue fever was enrolled in a structured protocol that included relevant hematological investigations. The diagnosis of dengue fever was based on the WHO criteria. All this data was recorded and entered in the predesigned, pre-tested, and semi-structured questionnaire. The relevant data was recorded, entered, and analyzed by SPSS version 24 for descriptive statistics and bivariate analysis.

## Results

During the study period of 6 months, 438 confirmed dengue patients were admitted, amongst which 254 were male (58%), and 184 were female (42%). The age of the children ranged from 04 months to 12 years, with a mean age of 8.03 years (SD + 3.13 years),

**Table 1: Demographic and Clinical Presentations**

<i>Demographic and Clinical Presentations of Dengue Cases</i>		
Gender	Frequency (n=438)	Percentage
Male	254	58
Female	184	42
Age (mean 8.03 years SD $\pm$ 3.13)		
Less than 1 year	15	3.4
1-4 years	78	17.8
5-8 years	114	26.1
9-12 years	231	52.7

In our study, out of 438 children, 254 (58%) were reported as uncomplicated dengue fever, 119 children (27%) developed dengue hemorrhagic fever and were managed accordingly. 65 children (15%) were into dengue shock syndrome and treated for this complication.

**Table 2: Frequency of Dengue Fever and Complications**

Classification	Frequency	Percentage
Dengue fever	254	58
Dengue hemorrhagic fever	119	27
Dengue shock syndrome	65	15
Total:	438	100

In our study, the main findings were thrombocytopenia (80.1%) and leucopenia (65.1%). leucocyte count was normal in only 59 patients (13.68%). 351 (80.1%) patients had Thrombocytopenia (platelets less than 100,000). 30 (6.9%) patients had a platelet count of less than 50,000. Most of the patients were positive for NS1 (70.3%). IgM was positive in 62.1% and IgG was positive in 14.8%. Enteric fever as a cop infection was seen in 30 patients, ALT was deranged in 42% of patients, and AST was elevated in 27.85%.

**Table 3: Laboratory Findings.**

LABORATORY HEMATOLOGICAL FEATURES			
Hematological parameter	Mean ( $\pm$ SD)	Minimum	Maximum
Total Leukocytes Count	$4.5 \times 10^3$ ( $\pm 2.5$ )	$1.1 \times 10^3$	$18.6 \times 10^3$
Hemoglobin	11.59 ( $\pm 2.32$ )	4.9 mg/dl	16.9
Platelets	$82.6 \times 10^3$ ( $\pm 48.1$ )	$9 \times 10^3$	$351 \times 10^3$
Hematocrit	33.84% ( $\pm 5.59$ )	18.9%	52.7%

ALT	104 mg/dl ( $\pm 55$ )	10.5 mg/dl	2251 mg/dl
AST	262 ( $\pm 295$ )	24 mg/dl	3598 mg/dl

COMPLETE BLOOD COUNT		
Blood Picture	Frequency	Percentage
Thrombocytopenia (platelets count <100,000)	351	80.1
Leukopenia (TLC <4000)	285	65.1
Anemia (Hemoglobin <10)	99	22.7
Platelet count <50,000	94	21.7
HCT >20% with platelet <50,000	97	22
<b>Dengue Serology</b>		
NS1 Ag Positive	308	70.3
Dengue IgM	272	62.1
Dengue IgG	65	14.8
Dengue IgM positive with NS1 negative	97	22.1

Thrombocytopenia, Leukopenia, HCT > 20% with Platelets <50,000, deranged LFTs, Hyponatremia, Hepato-splenomegaly, and Gall bladder wall thickness on Ultrasonography were seen significantly associated with Progression of Disease and Development of Complications.

**Table 4: Significant Laboratory Parameters for Development of Complications**

SIGNIFICANT LABORATORY PARAMETERS FOR DEVELOPMENT OF COMPLICATIONS					
Parameter	Variable	DF	DHF	DSS	P-Value
		N=254	N=119	N=65	
TLC (Mean $4.5 \times 10^3 \pm 2.5$ SD)	<4,000	165	77	43	0.991
	4,000 - 10,000	83	37	20	
	>10000	06	05	02	
Platelets (Mean $82.6 \pm 48.1$ SD)	>100,000	56	07	04	0.001
	50,000 - 100,000	95	102	48	
	<50,000	03	10	17	
HCT (33.84% $\pm 5.59$ SD)	>35	249	101	57	0.002
	<35	05	18	08	
ALT (Mean $104 \pm 55$ SD)	<100	234	89	40	0.000
	100 - 1000	20	29	21	
	>1000	00	01	04	
AST (Mean $262 \pm 295$ SD)	<100	234	89	40	0.000
	100 - 1000	20	29	21	
	>1000	00	01	04	

## Discussion

Dengue infections are asymptomatic in 75% of infected humans. A spectrum of disease, from self-limiting dengue fever to haemorrhage and shock may be seen. A complex interaction of host and viral factors occur and determine whether the infection will be asymptomatic, typical, or severe.<sup>2</sup> CBC parameters such as hemoglobin (Hb), hematocrit (Hct), WBC count, differential percentages of WBCs, and platelet count alter each day of fever in patients infected with dengue.<sup>10</sup> Pancytopenia may develop after 3-4 days of illness.<sup>3</sup> Early and accurate laboratory diagnosis of dengue virus infection is critical to effective patient management.<sup>5</sup>

Amongst the age and sex ratio, the majority of the children are in the age group of 8-12 years, boys more commonly affected than girls with male to female ratio of 1.2:1. A similar age group with a mean age (standard deviation) of 6.9+3.3 years and a higher male to female ratio of 1.2:1 was found in a study by Potha pregada S et al.<sup>18</sup> A study by Manoj Kumar et al. also shows a higher number of males affected with a male to female ratio of 1.54:1 among all seropositive cases.<sup>19</sup>

The most significant laboratory abnormality seen in our study was thrombocytopenia. A study has shown thrombocytopenia in 59.8%.<sup>11</sup> Another study has found thrombocytopenia in 67% of the cases.<sup>20</sup> Significant derangements in platelets were found in yet another study.<sup>21</sup> A study by Adel Hamed has documented thrombocytopenia in 74.45% of the patients.<sup>22</sup> As platelet counts decrease the complication rate increase and duration of hospital stay increase with decreasing platelet count. Platelet count can therefore be used to predict the complication and duration of hospital stay and hence better use of resources.<sup>23</sup>

In our study concomitant presence of leucopenia, raised haematocrit and low platelet count were commonly associated with dengue fever with warning signs. Leucopenia and differences in WBC count in dengue fever & dengue haemorrhagic fever have been found in a study by Juthatip Chaloe Wong et al., demonstrating leucopenia (WBC count < 5000 cells/mm) in 70.9% of the patients during the acute febrile phase (day 2, 3) of illness with the average value in the acute febrile phase of 4.38 and 4.49 in those who progressed to dengue haemorrhagic fever. Other studies have documented leucopenia in 66% of patients<sup>22</sup> and 26.5% of patients.<sup>11</sup>

In our study liver enzymes were in the range of 10 – 3500, with three children having a value of more than

3000. ALT & AST levels were significantly increased among severe dengue cases compared to uncomplicated dengue fever cases. An elevation in AST (45.1%) and ALT (17.6%) were found in a study by Ferede et al. (11). Kularatam et al. has found that AST and ALT levels begin to rise in the early febrile phase with the median concentration of AST of 746 u/L and ALT median concentration of 118 u/L.<sup>9</sup>

In our study, hemoglobin levels varied between 4.9 mg/dl and 16.9 mg/dl with a mean of 11.59 mg/dl ( $\pm$  2.32), while hematocrit varied between 18.9% and 52.7% with a mean of 33.84 ( $\pm$  5.59). Juthatip Chaloe Wong et al. have demonstrated that there is significantly higher hematocrit and higher hemoglobin levels than the control group from day 3 to day 10 with HB level of [14.3 gm/dl (13.98-14.55) vs 12.9 gm/dl (12.59-13.38)] and hematocrit [43.3% (42.29-43.89) vs 39.2% (38.42-40.67)] respectively.<sup>10</sup> A study by Udaya Ralpnawa et al. has shown Hb ranging from 9 to 18 gm/dl during the fifth day of illness with an average value of 13.2 and 14.04 among DF and DHF patients respectively, while the mean packed cell volume (PCV) value for DF and DHF were 39.29 and 47.49 respectively.<sup>24</sup> Rise in Hct is more distinct, rapid, and significantly higher in DHF than in DF.<sup>9</sup> In a study on various dengue syndromes a raised Hct was seen in 13.2% of patients at the time of presentation.<sup>20</sup> Endothelial dysfunction leading to increased vascular permeability is a hallmark of severe dengue leading to leakage of fluid into pleural and peritoneal cavities and shock.<sup>25</sup>

## Conclusion

Careful assessment and interpretation of hematological changes in pediatric dengue patients not only allow early diagnosis but also aid in adopting appropriate treatment.

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