Original Article

DOI: 10.21276/APALM.3156

Utility of Red Cell and Platelet Indices Evaluation of Severity of Dengue Infection

Keyuri Bharat Patel, Mustafa Fakaruddin Ranapurwala* and Anjali Nimeshkumar Patel

Department of Pathology, Pramukhswami Medical College, Bhaikaka University, Karamsad

ABSTRACT

Context: Dengue is the most common mosquito-borne viral illness in humans and transmitted by aedes aegypti. Infection may be asymptomatic or present with a mild febrile illness to a life-threatening shock syndrome and diagnosed by virological tests, serological tests, and complete blood count.

Aim: The present study was undertaken to evaluate the role of red cell and platelet indices to assess disease activity and severity of dengue infection.

Material and Methods: The present study was conducted at a tertiary level teaching hospital in Central Gujarat, India from November 2019 to August 2021.100 dengue positive cases and 100 controls (dengue negative case) were consecutively sampled. Epidemiological, clinical data and complete blood count were collected from online and offline registers of the Central Diagnostic Laboratory. Chi square test, independent sample T – test and Karl pearson coefficient of correlation were used for statistical analysis.

Results: Dengue cases have frequently presented with fever 32.65% or fever with chills / rigor 66.33%, headache 37.76%, body ache 44.90% and bleeding manifestations like petechiae 5.10% and bleeding from gum, nose and rectum 5.15%. while, 18% cases have ascites and 07% cases were found to have pleural effusion in dengue positive cases. Haemoconcentration, fall in total WBC count, platelet count and plateletcrit have significant statistical association with severity of dengue infection. Platelet count was directly proportional to plateletcrit in dengue positive cases.

Conclusion: Significant statistical association was presented between degree of leukopenia, thrombocytopenia, haemoconcentration and fall in plateletcrit with severity of dengue infection whereas plateletcrit has positive correlation with platelet count in dengue infection.

Keywords: *Dengue, White Blood Cells, Platelet Count, Plateletcrit*

Introduction

Fever is an important and one of the most common symptoms of patients presenting to emergency department. Acute undifferentiated febrile (AUFI) illness is defined as acute onset of fever with temperature of >38°C of less than two weeks duration without an obvious cause despite a meticulous history and physical examination. There are multiple causes of acute undifferentiated febrile illness. One of them are infectious febrile illness. The significant infectious illnesses are dengue fever, malaria, enteric fever, scrub typhus fever, leptospirosis and Japanese encephalitis[1].

Dengue, a Spanish alteration of the swahili word Ki-dinga pepo, is the most common mosquito-borne viral illness in humans. The illness was called “the water poison” and was associated with flying insects near water. Dengue is a febrile illness caused by infection with one of four dengue viruses transmitted by *aedes aegypti* or *aedes albopictus* mosquitoes during the taking of a blood meal[1,2]. Infection may be asymptomatic or present with a broad range of clinical manifestations including a mild febrile illness to a life-threatening shock syndrome.

Dengue is endemic in more than 100 countries. One estimate indicates 390 million dengue infections per year (95% credible interval 284–528 million), of which 96 million (67–136 million) manifest clinically (with any severity of disease). Another study, of the prevalence of dengue, estimates that 3.9 billion people, in 128 countries, are at risk of infection with dengue viruses[3].

Dengue infection has the potential to cause visceral bleeding, shock, and death. So, early diagnosis and recognition of complications is cornerstone in management. Even though, dengue infection admissions are common in paediatric age group, adult patient admissions have also increased in recent years.

According to WHO dengue fever diagnostic tools includes virological tests (that directly detect elements of the virus) and serological tests. The virological tests include – RT-PCR and virus induced protein called NS1 antigen. The serological test includes – ELISA with detection of IgG and IgM antibodies. By using a set of clinical and/or laboratory parameters, one sees a clear-cut difference between patients with severe illness and those with non-

severe illness like dengue without warning signs, dengue with warning signs and severe dengue[4].

Complete Blood Count (CBC) is one of the commonest laboratory tests that is requested for almost all the febrile cases. The most common findings are thrombocytopenia with concurrent haemoconcentration. However, with the advent of newer technologies of cell counts, platelet indices may act as a predictive biomarker for the presence and severity of the disease and decide on the need for red cell and platelet transfusions in dengue. Low platelet count, low MPV, low PCT, high PDW, and high P-LCR may be used as probable indicators for dengue in endemic areas and also as a predictor of severity of dengue infection[5].

The aim of the present study was to evaluate changes in red cell and platelet indices in dengue infections, and whether the changes in the same can be used as predictive biomarkers to predict severity of dengue infection.

Materials and Methods

Research Design: The present study is a tertiary care center based observational (prospective and retrospective) study conducted at the Central Diagnostic Laboratory at Department of pathology, Shree Krishna Hospital, Karamsad, Gujarat during period of November 2019 to August 2021.The study is designed to use the red cell indices and platelet indices generated by the automated hematology analyzer as an additional tool for diagnostic/ prognostic purpose in dengue infections.

Source of Data: Febrile patients of all ages and both genders with a clinical suspicion of dengue from OPD and ICU patients were included. The patients would be clinically classified into Dengue without warning signs, Dengue with warning signs, Severe Dengue. Demographic details, history and the clinical presentation data was collected from the indigenously developed online HMIS (SOLACE) shown in Figure 1.

Methods for Diagnosis: This is a prospective and retrospective study of 200 samples both EDTA and PLAIN vacuettes collected at hematology, biochemistry and microbiology section of Central Diagnostic laboratory at Department of Pathology, Shree Krishna hospital, Karamsad.

Plain vacuettes were used for serological dengue detection using three rapid diagnostic methods including NS1 antigen, IgM and IgG antibodies test Additional serum albumin levels were also done.

EDTA vacuettes were used for complete blood count and platelet indices were evaluated by using automated hematology analyzer XN 350/550.

Statistical Analysis: In present study, multiple statistical analysis were used for different variable analysis. analysis were performed by using STATA 14.2.

Comparison of red cell parameters and platelet parameters were done with dengue cases and correlation between red cell parameters and platelet indices were done by using Karl pearson coefficient of correlation.

Results and observations: The present study comprises a total of 200 cases, out of which, 100 were dengue positive cases and 100 dengue negative cases(as control group) were included in the study.
In present study, Population of 1 month to 85 years of age group was included, amongst which Dengue positive cases were more commonly seen in age group of 20-29 years having Males outnumbered females with Male: Female ratio of 1.89:1.0.

Distribution of dengue serology results was shown in **Table 1**.

Out of 98 cases, 48 cases were having triad of symptoms comprised of fever or fever with chills/rigor, bodyache and headache found to have NS1 antigen positive.

The most frequent clinical presentation were Fever with chills (66.33%) and Bodyache (44.90%) followed by Headache (37.76%), Fever (32.65%), Vomiting (24.49%), Weakness (18.37%), Abdominal pain (15.31%) and Cough/ cold (6.12%) in decreasing order.

Of the 100 dengue positive cases a total of 05 cases had petechiae, 02 has ecchymoses, 04 cases had purpura, 11 cases had bleeding from other sites and 03 cases had episodes of hematemesis. And total of 11 cases had pleural effusion and 25 had ascites.

According to WHO, dengue infections categorized into dengue negative cases, dengue without warning sign, dengue with warning sign and severe dengue infection which are shown in **Table 2**.

All the samples were additionally run on a Sysmex XN series automated haematology analyzer (350 or 550) and studied for complete blood counts and platelet indices.

In present study, out of 200 cases, amongst which 42 cases machine couldn't detect platelet indices, out of these 42 cases, 21 cases were dengue positive.

Correlation of haematological parameters are shown in below **Table 3:**

Considering biochemical parameter, serum albumin was compared with evidence of plasma leakage. In present study out of 200 cases, 142 case underwent the test for

serum albumin from which 68 cases were dengue positive. There was statistically significant association were found between fall in the serum albumin and ascites in dengue positive cases. While serum albumin is decreased significantly in dengue positive cases with pleural effusion, but no significant association were found between serum albumin and pleural effusion.

Karl Pearson Correlation was used to show correlation between parameters like red cell indices, platelet count and total WBC count with platelet indices in dengue positive cases. Karl Pearson Correlation(r) value taken for parameters evolution. In present study, according to Karl Pearson Correlation, haemoglobin value were directly proportional to mean platelet volume and plateletcrit, while inversely proportional to platelet distribution width in dengue positive cases.

Platelet count was inversely proportional to mean platelet volume and platelet distribution width, which is surrogate indicator of increased megakaryocyte activity in bone marrow in dengue positive cases in present study. The platelet count is directly proportional plateletcrit in present study.

In present study, haematocrit value is inversely proportional to mean platelet volume, platelet distribution width and Plateletcrit in dengue positive cases.

Total WBC count is directly proportion to platelet distribution width and plateletcrit for dengue cases and inversely proportional to mean platelet volume.

In present study, rise in hemoglobin and hematocrit, leukopenia and thrombocytopenia showed statistically significant association between dengue without warning sign, dengue with warning sign and severe dengue categories.

While, mean platelet volume and platelet distribution width shows no statistically significant association to different dengue categories, while fall in plateletcrit found to have statistically significant association in these dengue categories. Significantly low plateletcrit were found in severe dengue infection.

Table 1: Dengue serology results (n=100).

Serology groups	NS1 antigen	IgM antibody	IgG antibody	Total
Only NS1 positive	89	--	--	89
Both NS1 and IgM positive	09		--	09
Only IgG positive	--	--	02	02

Table 2: Categories of dengue infections

Categories			Cases
Dengue Negative			100
Dengue Positive (n=100)	**Without warning sign**		46
	With warning sign		43
	Severe dengue	**Severe plasma leakage**	08
		Severe bleeding	02
		Organ involvement	01

Table 3: Correlation of laboratory parameters with Dengue serology test.

Laboratory parameters	Serology results	Cases	Mean (SD)	P-value
Hemoglobin	Positive	100	13.26(8.42)	0.005
	Negative	100	10.76(3.16)	
Hematocrit	Positive	100	37.77(7.94)	<0.001
	Negative	100	32.50(8.89)	
Total WBC Count	Positive	100	5.81(6.15)	<0.001
	Negative	100	10.51(7.26)	
Platelet count	Positive	100	123.32(9.00)	0.0001
	Negative	100	188.95(13.02)	

Laboratory parameters	Serology results	Cases	Mean (SD)	P-value
Mean platelet volume	Positive	79	10.47(1.00)	0.19
	Negative	79	10.23(1.27)	
Platelet distribution width	Positive	79	11.66(2.63)	0.14
	Negative	79	10.97(2.94)	
Plateletcrit	Positive	79	0.14(0.08)	<0.001
	Negative	79	0.22(0.10)	

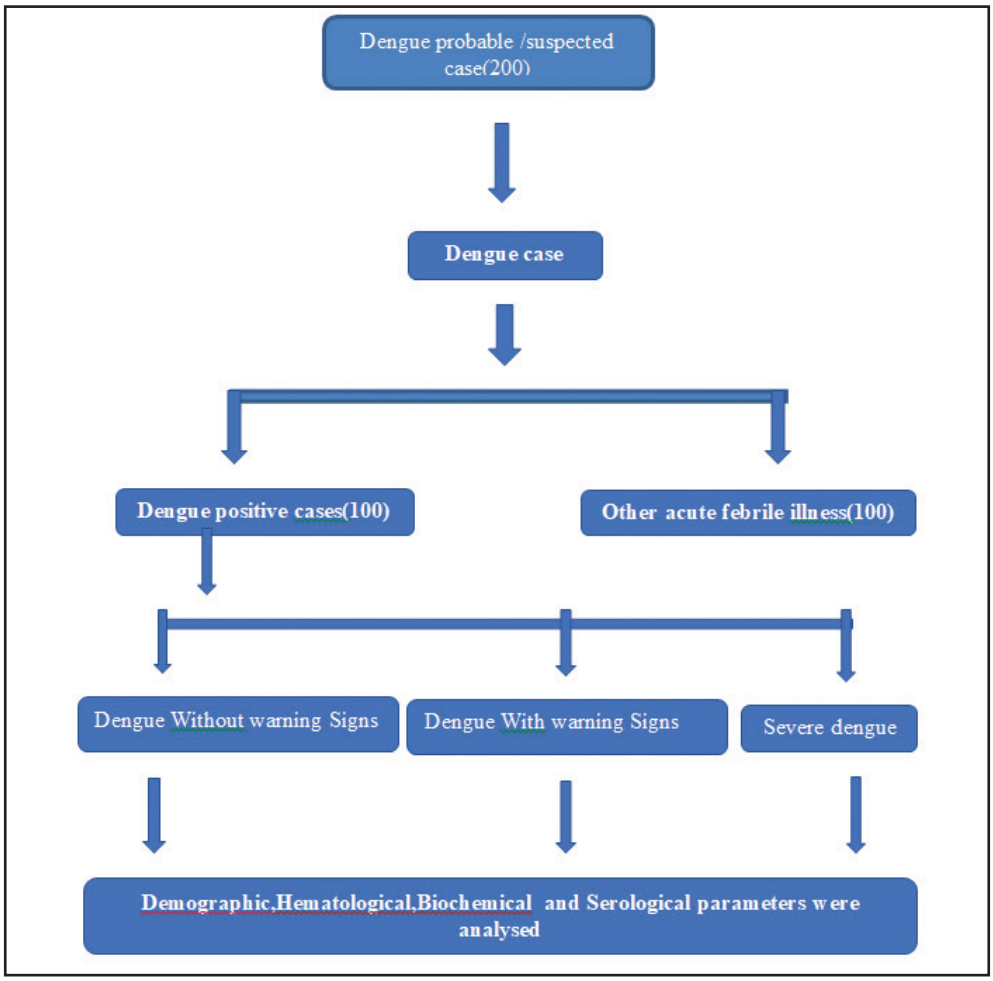

Fig. 1 : Sample size with inclusion and exclusion criteria.

Discussion

The incidence of dengue fever has been the rising trend. The true incidence cannot be determined since the hospitalized patients represent only the tip of the iceberg those with clinical symptoms amidst the vast majority of the population who have subclinical infection.

This study was primarily undertaken to asses changes in red cell & platelet indices and if they can be used as additional tool for diagnosis/ prognostic purpose in dengue infection.

In the present study, out of 100 dengue positive cases, 89 cases were only NS1 positive, 02 cases were only IgG positive and 09 cases were NS1 and IgM both positive. **Navya B.N et al (2016)**[6] study with 100 dengue positive cases out of which 90 cases show NS1 positive, 08 cases show only Ig G positive and 02 cases show all positive (NS1, IgG and IgM).

Dengue affects humans of all age groups worldwide. In some parts of the world, it is mainly a paediatric health

problem. In the present study among 100 patients 70 (70%) were males ,30 (30%) were females having dengue positivity and male to female ratio was 2.3: 1.0. Mean age of presentation was 36 years A study was done by **Athira PP et al (2018)**[7], where total 211 children were clinically suspected on the admission as dengue fever, 34 of these were serologically confirmed dengue positive among them 20 (59%) were male and 14(41%) were female and male to female ratio was 1.4: 1.0. Mean age of presentation was 8 years.

Clinical Presentation : The most frequent clinical presentation in present study were fever or fever with chills /rigor (98%) and bodyache (44.90%) followed by headache (37.76%), vomiting (24.49%), weakness (18.37%), abdominal pain (15.31%) and cough/cold (6.12%) in decreasing order. Of the different bleeding signs identified in dengue positive patients, common presentation observed were petechiae (07%), bleeding from any site (06%), purpura (04%) and ecchymosis (3.0%). A study done by **Wayez A, et al. (2020)**[8] shows fever was the major complaint, seen in almost all patients at presentation (100% cases). It was accompanied by vomiting (10.38%), gum bleed (9.43%), generalized bodyache (8.49%), rash (6.6%), epistaxis (3.77%) and pruritus (2.83%).

Ramamoorthy S et al (2017)[9] found that fever (92%), vomiting (44%), headache (20%) and abdominal pain (34%) are the most common presenting illness. Among all bleeding manifestations, melena (48%), petechial haemorrhage (28%) are common.

In present study, Ascites & Pleural Effusion were explored for as an evidence of plasma leakage which were 7.14% and 18% respectively**. Dr. Abhinand s. Bedge et al (2010)**[10] found that 84% patients having pleural effusion and 88% patients having ascites.

Laboratory parameters:

The present study shows an increasing trend in haemoglobin and hematocrit with dengue positivity showed a significant association with dengue by NS1 antigen. **Rai A. et al. (2019)**[11]shows rise in haemoglobin compared to control group which have statistically significant association with dengue positive cases. While other two studied done by **Mukker P et al (2018)**[12] and **Jenny C. Cardenas et al (2021)**[13] does not show statistically significant association with dengue cases.

Total WBC Count and platelet count showed a significant association with dengue by NS1 antigen cases showing a decrease in value in the positive cases as compared to the negative cases in the present study. **Rai A. et al. (2019)**[11] shows fall in total WBC count and platelet count which have statistically significant association with dengue positive cases. Other study done by **Jenny C. Cardenas et al (2021)**[13] does not show statistically significant association with dengue cases.

In present study, mean platelet volume and platelet distribution width shows no statistical significant association with dengue positive cases though there was mild decrease in MPV and increase in PDW as compared to dengue negative cases. While plateletcrit value were decreased significantly in positive cases as compared to control cases amongst the NS1 antigen cases thus found significant statistical association in dengue positive cases.

Bashir AB et al (2015)[14] found that MPV was decreased in dengue positive cases and was normal in control group. PDW was normal in control group while it was increased in dengue infection. **Chiranth S.B et al (2019)**[15] observed that 83% had mean platelet volume below 9fl, 68% had platelet distribution width below 18, 64% had plateletcrit (PCT) below 0.1%, from which PCT showed a significant correlation with dengue fever.

The Karl Pearson Correlation, observed that platelet count was inversely proportional the to mean platelet volume and platelet distribution width, which is a surrogate indicator of increase megakaryocyte activity in bone marrow activity in dengue positive cases. While platelet count is directly proportional to plateletcrit in present study. **Wayez A et al (2020)**[8] observed the value of MPV increases as the platelet count increases that suggests a direct relationship of platelet count with mean MPV, while negative correlation between the mean PDW and the platelet count was found so that low platelet count was associated with high PDW and PCT shows a positive correlation between the PCT and the low platelet count. The study done by **Bashir AB et al. (2015)**[14] observed that, there were statistically significant correlation between mean platelet volume and platelet distribution width with thrombocytopenia.

According to WHO 2009 recommendation, in present study, out of 100 cases, it observed that 46 cases fall under dengue without warning sign, 43 cases were having dengue with warning sign while 11 cases have severe dengue. These findings were comparable with other study done by **Athira pp et al (2018)**[7]. 16 were identified as dengue with warning signs, 7 as dengue without warning signs, while 11 were identified as severe dengue.

There was fall in total WBC count, platelet count and rise in haemoglobin and haematocrit shows statistically significant association to differentiated dengue without warning sign vs dengue with warning sign vs severe

dengue in present study. While **Athira pp et al (2018)**[7] observed that, no statistically significant association were found for fall in Total WBC count, Platelet count, Rise in haemoglobin and Haematocrit in dengue without warning sign, dengue with warning sign and severe dengue in their study.

Limitations of the study:
With the present study, there were a few limitations, that were noted:

a) Very low platelet count (<20,000), yielded no platelet indices and hence, the same couldn't be studied.

b) The number of patients with severe dengue were few and hence, they could not be studied in detail.

We would have wanted more subjects with varied manifestations to assess the correlation of laboratory parameters with clinical severity.

Conclusion

Bearing in mind the aim of the present study:

A significant association is noted between leukopenia, thrombocytopenia and increase in haemoglobin and haematocrit value with occurrence of dengue.

Haemoconcentration, leukopenia, thrombocytopenia and decrease in plateletcrit have strong correlation with severity of dengue. Amongst the platelet indices plateletcrit has a statistical significance with occurrence of dengue.

Low plateletcrit and platelet count with high mean platelet volume and platelet distribution width are associated with severity of dengue

Funding

None received

Competing Interests

None

Reference

1. Kalra V, Ahmad S, Shrivastava V, Mittal G. Quantitative and volume, conductivity and scatter changes in leucocytes of patients with acute undifferentiated febrile illness: a pilot study, *Transactions of The Royal Society of Tropical Medicine and Hygiene*, Volume 110, Issue 5, May 2016, Pages 281–285
2. Guzman MG, Harris E. Dengue. Lancet. 2015 Jan 31;385(9966):453-65.
3. Brady OJ, Gething PW, Bhatt S, Messina JP, Brownstein JS, Hoen AG et al. Refining the global spatial limits of dengue virus transmission by evidence-based consensus. PLoS Negl Trop Dis. 2012;6: e1760.
4. World Health Organization [home page on the Internet/ Newsroom/Factsheet/Details/Dengue and severe dengue], c2020.
5. Kantharaj A. Role of platelet and red cell indices as a predictive tool for transfusion in dengue. Glob J Transfus Med 2018;103.8
6. Navya BN, Patil S, Kariappa TM. Role of platelet parameters in dengue positive cases - an observational study. Int J Health Sci Res. 2016; 6(6):74-78
7. Padmanabhan P Athira et al., Retrospective Study of Pediatric Dengue Cases in a Tertiary Care Hospital in Southern India. Journal of Clinical and Diagnostic Research. 2018 Jul, Vol-12(7): SC01-SC06
8. Wayez A et al (2020) Study of platelet indices in dengue fever with thrombocytopenia and correlation of immature platelet fraction (IPF) with platelet recovery. Arch Hematol Case Rep Rev 5(1): 001-005
9. Sudhakar Ramamoorthy et al, Comparison of Platelet Indices with Platelet Count to Predict Bleeding Tendency in Seropositive Dengue Case; JMSCR Volume 05 Issue 12 December 2017:31639-31641.
10. Dr. Abhinand s. Bedge al. "clinical perspective of dengue among adults" department of general medicine al-ameen medical college, bijapur,2012
11. Rai A et al. Correlation between haematological and serological parameters in dengue patients an analysis of 2022 cases. Trop J Path Micro 2019;5(8):547-554
12. Mukker P, Smitha kiran et al platelet indices evaluation in patients with dengue fever. Int J Res Med Sci.2018 Jun;6(6):2054-2059
13. Cardenas JC et al. Laboratory Findings in Patients with Probable Dengue Diagnosis from an Endemic Area in Colombia in 2018. Viruses 2021, 13, 1401
14. Bashir AB et al. Role of Platelet Indices in Patients with Dengue Infection in Red Sea State, Sudan International Journal of Science and Research Volume 4 Issue 1, January 2015,1573-1576
15. Chiranth S.B et al. Platelet Indices and the Severity of Dengue Infection in Children; J Pediatr Res 2019;6(3):242-246

***Corresponding author:**
Dr. Mustafa Fakaruddin Ranapurwala, Assistant Dean, Diagnostic Services, Central Diagnostic Laboratory, Pramukhswami Medical College & Shree Krishna Hospital, Bhaikaka University, Karamsad- 388325
Phone: +91 9898982709
Email: dr.mustafa.r@gmail.com

Financial or other Competing Interests: None.

Date of Submission : 25/01/2022
Date of Final Revision : 21/04/2022
Date of Acceptance : 05/05/2021
Date of Publication : 31/05/2022