Immature platelet fraction and platelet counts changes in dengue fever patients

by Rori Indras Puspita

Submission date: 14-Oct-2019 03:11PM (UTC+0800)
Submission ID: 1192393886
File name: armenian_Vol._13,_No._1,_2019_Immature.pdf (272.68K)
Word count: 3547
Character count: 17754

THE NEW ARMENIAN MEDICAL JOURNAL
Vol.13 (2019), No 1, p.64-68

IMMATURE PLATELET FRACTION AND PLATELET COUNTS CHANGES IN DENGUE FEVER PATIENTS

Rori Indras Puspita, Usman Hadi*, Muhammad Vitanata Arfijanto, Musofa Rusli, Bramantono, Muhammad Miftahussurur

Department of Internal Medicine, Faculty of Medicine - Dr.Soetomo Teaching Hospital, Universitas Airlangga, Surabaya, Indonesia

Received 15.12.2018; accepted for printing 10.01.2019

Abstract

Background: *The clinical course of Dengue Hemorrhagic Fever (DHF) is difficult to predict. An improvement of platelet count is one of the recovery parameters in DHF patients. Immature platelet fraction (IPF) can be used to estimate platelet count changes in the next 1-2 days in DHF patients. We analyzed the correlation between immature platelet fraction and platelet count changes in DHF patients patients.*

Methods: *The cross-sectional observational analytical was used in this research. Thirty adult DHF patient with were enrolled in this study. IPF and platelet count change of each patient were measured. , then correlation analysis between immature platelet fraction and platelet count changes in DHF patients was analyzed using Pearson test.*

Results: *There were 30 DHF patients consisting of 18 (60%) male and 12 (40%) female with mean age of 24.83 ± 9.18, mean immature platelet fraction 11.77 ± 5.5%, and mean platelet count change 29,547 ± 45,244.12 / µl. From Pearson correlation test $p < 0.001$ and $r = 0.746$ were obtained, suggesting strong correlation.*

Conclusion: *There was a strong correlation between IPF and platelet count changes in DHF patients.*

Keywords: *Dengue hemorrhagic fever, immature platelet fraction, platelet count change*

Introduction

Clinical manifestations of dengue virus infection highly vary from asymptomatic, non-specific fever, dengue fever to dengue shock syndrome (1, 2). Thrombocytopenia is one of the simplest criteria of WHO that plays a role as a clinical diagnosis of DHF. In DHF patients thrombocytopenia may occur due to suppression of platelet production in the bone marrow, increased platelet consumption caused by disseminated intravascular coagulation, platelet destruction caused by increased apoptosis, lysis by the complement system and the presence of antiplatelet antibodies (3-7). The clinical course of DHF disease is difficult to predict, patients with clinical and early laboratory conditions seem to be healthy in a short time that may get worsened and untreated. Conversely, many DHF patients with clinical and laboratory conditions seem to be healed and survived the disease (8). Improvement of platelet count is one of the recovery parameters in DHF patients (1).

Dengue virus infection continues to increase in prevalence every year, it is estimated there are 50 - 100 million cases of Dengue virus infected and 2.5 billion people in high risk (1). In 2006, there was a dengue fever epidemic in India by 12.317 cases with 184 deaths. In 2010, 2012, 2013 there were 28.292, 50.222, and 75.808 cases, respectively.in by. WHO stated that Case Fatality Rate has declined from 3.3% in 1996 to 0.4% in 2010 after the WHO guidance guidelines (1). In 2013, approximately 96 million cases of dengue infections occured each year, this increased more than three times compared to the number of cases in 2012 according to WHO data (9). In 2015, in East

Address for Correspondence:
Prof. Usman Hadi MD, Ph.D
Departement of Internal Medicine, Faculty of Medicine, Dr. Soetomo Teaching Hospital, Universitas Airlangga, Surabaya 60285, Indonesia
Tel.: +6231-550-1177
E-mail : muhammad-m@fk.unair.ac.id

Java, there was an increase in dengue cases by 46% and 15 districts/cities experienced outbreaks as the number of dengue cases in the region doubled compared to the same month in 2014 (10).

In the condition of thrombocytopenia without bone marrow disorder, new platelets are more widely released from megakaryocyte, larger platelets with high RNA content are called reticulated platelets (immature platelets). Immature platelet fraction (IPF) is an additional parameter that can be monitored to predict the recovery of platelet count by measured percentage of immature platelet to the total platelet count. The normal values in healthy individuals were assigned 1.1 to 6.1% (11). IPF was examined using Sysmex hematology analyzer with the flowcytometry method. Immature platelet fraction can be used to estimate platelet count recovery time in the next 1-2 days (12).

Several research revealed that IPF had a strong relationship with platelet count reconstitution in dengue infection patients with evidence that 93.75% of patients had recovered thrombocytopenia within 24-48 hours after IPF increased (13). IPF was found higher in dengue hemorrhagic fever compared to dengue fever, whereas platelet count was lower in dengue hemorrhagic fever than dengue fever. IPF of dengue hemorrhagic fever on the third day was significantly different from IPF on the first day of hospitalization (14).

IPF was higher in patients with lower platelet counts (14). Patients with thrombocytopenia where IPF ≥6.25 indicated that there was a 67% chance of an increase in platelet count by 20,000 within 48 hours and an IPF ≥10.6 score indicated that there was a 100% chance of platelet increase by 20,000 within 48 hours (15). If we know the correlation between immature platelet fraction with platelet count change then we can use IPF for monitoring the change of platelet count in DHF patients. Therefore, we wanted to know the correlation between immature platelet fraction and platelet count change in dengue hemorrhagic patients.

METHODS

This study was an analytical observational with cross-sectionaldesign. Inpatient patients in the Tropic-Infectious Disease Room of Internal Medicine in Dr.Soetomo Teaching Hospital Surabaya diagnosed with DHF according to WHO SEARO 2011 criteria that met inclusion but not exclusion criteria were the subjects of this study.and does meet. The inclusion criteria were as follows: patients with DHF based on WHO 2011, fever lasted less than 6 days, aged 17-60, approved to participate in this study by signing an informed consent. Subjects suffering from other medical disorders that cause thrombocytopenia (leukemia, aplastic anemia, SLE, SH, ITP) was exclusion criteria. Subjects were selected by consecutive sampling until the sample size requirement was fulfilled.

The subjects filled informed consent, underwent anamnesis, physical and laboratory examination, venous blood sampling by 3 ml for platelet fraction examination, and measurement immature platelet fraction at 4/5th day fever. Immature platelet fraction was examined at Pramita Pramita Hospital Laboratory, with repeated thrombocyte measurement in the next two days on at 6/7th day fever. Immature platelet fraction was examined using Sysmex autoanalyzer haematology and expressed in % unit. Data of platelet count change and immature platelet fraction were recorded and analyzed..

The data were analyzed with descriptive statistics and presented in the form of frequency distribution tables and diagrams. The correlation between immature platelet fraction and platelet count change were analyzed using Pearson correlation test if data were normally distributed, or using Spearman's test if the data distribution were not normal.. Interpretation of correlation test was determined based on p-value, correlation strength, and direction of correlation.

RESULTS

In this study 30 adult patients diagnosed with DHF based on serology NS1 or positive IgM Dengue were enrolled, with the youngest patient aged 17 and the oldest aged 50. The highest proportion of study subjects was found in the age group of 17-27 years. The general characteristics of subjects in this study are shown in table 1.

From the results of IPF examination on 30 subjects of DHF research it was obtained that the data distribution based on the Shapiro-Wilk normality test was normal with an average of 11.77 ± 5.5%. From the platelet count examination on the 4th/5th day of fever it was obtained that the data distribution based on the Shapiro-Wilk normality test was

TABEL 1

General Characteristics of Patients

General Characteristics		Results
Sex	Male	18 (60%)
	Female	12 (40%)
Age (year)	Rerata ± SD	24,83 ± 9.18
Serology Test	NS 1+	15 (50%)
	Ig M+	15 (50%)
Degrees of DHF	I	10 (33,33%)
	II	16 (53,33%)
	III	4 (13,33%)
	IV	0

abnormal, with mean of 36.677.33 ± 25.318.95 (/ µl), median 28.465 (/ µl) and minimum value 3.000 (/ µl) and a maximum value of 92.140 (/ µl). While the results of the 6th / 7th platelet count of the heat of the study subjects based on Shapiro-Wilk normality test had normal distribution, with mean of 66.224.33 ± 38.525.27 (/ µl), median 72.440 (/ µl) and minimum value 11.360 (/ µl) and a maximum value of 157.300 (/ µl).

The change of platelet count of study subjects after analyzed using paired t-test showed significant difference with p = 0,001 (significant when p <0,05), meaning that there was the significant difference in platelet count of research subjects. Based on the result of thrombocyte count examination on 30 subjects of DHF distribution the value of platelet count change from the Shapiro-Wilk normality test showed normal distribution, with mean value of platelet count change of 29.547 + 45.244,12 / µl, median 24.105 (/ µl) and minimum value -75.930 (/ µl) and a maximum value of 142.890 (/ µl).

In the data normality test, Shapiro-Wilk concluded that the data spread normally if the value of p-value obtained was greater than the significance level of 5% (> 5%). The result of normality test of data to IPF and platelet count change was obtained p-value value of 0.976 and 0.314, suggesting that distribution of IPF distribution and platelet count change were normal.

Based on the result of the IPF data and normal platelet count change, then to analyze the correlation between IPF and platelet count change is used the parametric correlation of Pearson. Conditions used is a correlation can be concluded meaningful if the value of p-value obtained is smaller than 5% significance level (<5%). Results of analysis of the relationship between IPF and platelet count change in this study by using Pearson correlation analysis obtained Pearson r value of 0.746 with p-value 0.000. The value of r was 0.746 which showed a strong correlation. IPF relationship with platelet count change in this study waspositive or a meaningful direction with increasing levels of IPF then platelet count changes will increase.

DISCUSSION

This study followed 30 DHF patients mostly male, with the ratio of 1.5: 1. The subjects in this study had an average age of 24.83 years, the youngest patient was 17 years old, while the oldest patient was 50 years old, almost the same as the previous research, the mean age of 27.23 years with the age range between 14 -54 (14).

The sample of this research was 30 dengue fever patients with the first degree of dengue fever by 10 (33,33%), DHF II patients were 16 (53,33%), DHF III patients was 4 (13,33%) and no patient DBD degree IV. Serologic diagnosis with NS1 + by 15 patients (50%) and IgM + by 15 patients (50%). In this study, serologic examination for diagnosis of DHF was performed NS1 in patients who came with 1st -4th day of fever, while patients who came with the 5th -day of were examined the IgM Dengue.

From the examination of platelet count on the 4th/5th day of fever in this study, the distribution was found to be abnormal, with a median of 28.465 /µl and a minimum value of 3.000 /µl and a maximum value of 92.140 /µl. This result was different from examining platelets of DHF patients on the first day of admission who received platelet mean of 77.250 ± 38.041 /µl (14). While the result of thrombocyte count of the 6th/7th day of heat has a normal distribution with a mean of 66.244.33 ± 38.525.27 /µl. This result way different from the study examining the platelet count of DHF patients on the 3rd day of admission to the hospital who received platelet mean of 94.150 ± 62.116 /µl (14).

In this study, the result of IPF examination, based on Shapiro-Wilk normality test was normal with the mean of 11.77 ± 5.5%. This result was different from the study that examined the IPF in 20 DHF patients on the first day of admission who received an average IPF of 4.65 ± 3.87% (14).

In this research, the result of IPF average higher

than another research result. This was because the mean of platelet count in the patient of this research sample was lower. The lower the platelet count in dengue patients the patient's IPF score will be higher during the recovery phase in the course of DHF as a compensation for the condition of thrombocytopenia occurring.

Based on the result of platelet count calculation on 30 subjects of DHF research from Shapiro-Wilk normality test it was found that the distribution of platelet count value was normal, with the mean value of platelet count change of 29.547 ± 45.244.12 /µl. The change of platelet count is obtained from platelet count on day 6/7 heat minus platelet count in hot day 4/5. No previous research has evaluated platelet count change, the study that obtained a mean platelet count of DHF patients on the first day of hospital admission 77.250 ± 38.041 /µl and day 3 was hospitalized 94.150 ± 62.116 /µl with mean of platelet count change obtained from the average of 3rd day platelet count in hospital reduced the mean of platelet count in the first day of hospital admission 16.900 /µl (14). The average of platelet count in this research was 29.547 /µl greater than the average value of platelet count change by 16.900 /µl (14).

The average platelet count change in the first examination in this study was lower so that when the recovery phase occured in the course of dengue disease. A larger increase in platelet count was measured at the second examination to return to normal platelet count value (14). The average of platelet count in the first examination in this study was lower because of the possibility of the examination was performed on the heat of the day to 4/5. Then, the platelet count of DHF patients tend to be low whereas the first platelet count examination performed at the time of DHF patients entered the hospital the first day that could occur in the heat of day to any in the course of dengue disease (14).

The correlation between IPF and platelet count change in DHF patients in this study was obtained r = 0.746 with the p-value of 0.000 (α = 5%). Based on the results of statistical calculations concluded that there was a correlation between IPF and platelet count changes in patients with DHF in Dr. Soetomo General Hospital Surabaya. Pearson correlation coefficient value (r) of 0.746, suggesting a correlation between IPF and platelet count change in DHF patients in Dr. Soetomo General Hospital Surabaya was strong. The direction of a positive or unidirectional correlation means that when IPF increased, the higher the then the platelet count changes would also increase. As many as 84.3% of patients experienced platelet count elevation within 24 hours after IPF peak increase it could be concluddd that IPF can be used to monitor platelet count reconstitution in DHF patients. 120 DHF patients get if IPF> 6.25% then there is a 67% chance of a platelet increase of 20.000 /µl within 48 hours, and if IPF> 10.6% there is a 100% chance of a 20.000 /µl increase in platelet in 48 hours (15).

The research that has been performed to analyze the correlation between IPF and platelet count in DHF patients who entered the hospital on the first day and between IPF and platelet count in DHF patients who were hospitalized on day 3 of 20 dengue fever patients (14). The correlation between IPF and platelet count in dengue patients admitted to hospital on the first day was r = -0.662 with p = 0.001, and on day 3 admitted hospital r = -0.675 with p = 0.001 (14). This study shows that the lower the platelet count will be the higher the value of IPF at the same time.

In dengue patients with thrombocytopenia conditions, the value of IPF will increase with recovery in the bone marrow that will increase platelet count in peripheral blood 1-2 days later. In patients with ITP-induced thrombocytopenia where abnormalities that occured were platelet destruction in peripheral blood circulation caused by an autoimmune process and no disturbance in the bone marrow, the IPF score will be high since the onset of thrombocytopenia. In ITP patients high IPF values were not followed by an increase in platelet count in peripheral blood circulation in the next 1-2 days because the process of platelet destruction in peripheral blood circulation occured more than platelet production from bone marrow.

The results of this study indicated that the research samples with IPF value were higher then we get an increase in platelet count is also higher. While in the sample of research with low IPF value obtained the counting of platelet count. The increase or decrease in platelet count in line with the occurrence of plasma leakage according to the clinical course of DHF patients. Patients with platelet count changes are still decreasing in line with the occurrence of leakage plasma is still worsening, while patients with platelet

count changes that increase in line with the improved plasma leakage. Fluid therapy in dengue patients still experiencing worsening plasma leakage should be adequate to avoid falling under shock, while fluid therapy in dengue fever patients with improved plasma leakage should not be overly aggressive and should be alert because once plasma leakage improves there will be a shift back fluid to the intravascular and may occur overload when fluid therapy is too aggressive. So with the data of IPF on DHF patients are strongly correlated positively with platelet count changes in line with the occurrence of plasma leakage it can be used as one of the considerations of fluid therapy in patients with DHF..

CONCLUSION

There was a strong correlation between IPF level and platelet count change in DHF patients. It suggested that IPF to be used for monitoring DHF due to its ability to early predict platelet count changes in the next 1-2 days.

REFERENCES

1. WHO S. Comprehensive Guidlines for Prevention and Control of Dengue and Dengue haemorrhagic Fever,. edition Rae, editor: WHO; 2011. 1-196 p.
2. *Martina BE, Koraka P, Osterhaus AD.* Dengue virus pathogenesis: an integrated view. Clin Microbiol Rev. 2009;22(4):564-81.
3. *Srichaikul T.* Hematologic Changes in Dengue Hemorrhagic Fever. Journal Hematology Transfusion Medicine. 2013;24(1):47-55.
4. *de Azeredo EL, Monteiro RQ, de-Oliveira Pinto LM.* Thrombocytopenia in Dengue: Interrelationship between Virus and the Imbalance between Coagulation and Fibrinolysis and Inflammatory Mediators. Mediators Inflamm. 2015;2015:313842.
5. *Hottz ED, Oliveira MF, Nunes PC, Nogueira RM, Valls-de-Souza R, Da Poian AT, et al.* Dengue induces platelet activation, mitochondrial dysfunction and cell death through mechanisms that involve DC-SIGN and caspases. Journal of thrombosis and haemostasis : JTH. 2013;11(5):951-62.
6. *Assinger A.* Platelets and infection - an emerging role of platelets in viral infection. Frontiers in immunology. 2014;5:649.
7. *Lin CF, Wan SW, Cheng HJ, Lei HY, Lin YS.* Autoimmune pathogenesis in dengue virus infection. Viral immunology. 2006;19(2):127-32.
8. *Soegijanto S.* Patogenesa dan Perubahan Patofisiologi Infeksi Virus Dengue 2006. Available from: http://www.pediatrik.com.
9. *Guzman MG, Harris E.* Dengue. Lancet. 2015;385(9966):453-65.
10. *Kemenkes RI.* 2015. Available from: http://www.depkes.go.id/article/view/15013000002/kemenkes-terima-laporan-peningkatan-kasus-dbd-di-jawa-timur.html.
11. *Briggs C KS, Hart D, Oguni S, Machin SJ,.* Assesment of immature platelet fraction(IPF) in peripheral Thrombocytopenia. British Journal of Laboratory Hematology. 2004;126:93–9.
12. *Hoffmann JJ.* Reticulated platelets: analytical aspects and clinical utility. Clinical chemistry and laboratory medicine. 2014;52(8):1107-17.
13. *Dadu T SK, Joshi M, Khodaji S,.* Evaluation of the immature platelet fraction as an indicator of platelet recovery in dengue patients. International Journal Laboratory Hematology. 2013;36:499-504.
14. *Muhashonah I SJ, Wardhani P, Aryati,.* Immature platelet fraction di Demam Dengue dan Demam Berdarah Dengue. Indonesian Journal of Clinical Pathology and Medical Laboratory,. 2012;21(1):40-4.
15. *Suman FR DCL, Rejendran R, Varadarajan S,.* Dengue: platelet and immature platelet dynamics a study done at a tertiary care centre fromSouth India. International Journal of Recent Trends in Science AndTechnology. 2014;12(3):620-3.

Immature platelet fraction and platelet counts changes in dengue fever patients

ORIGINALITY REPORT

3%	2%	3%	0%
SIMILARITY INDEX	INTERNET SOURCES	PUBLICATIONS	STUDENT PAPERS

PRIMARY SOURCES

1	journals.plos.org Internet Source	1%
2	Nur Atik, Al Hadi Amrullah, Andri Reza Rahmadi. "Guava leaf juice effect towards number of megakaryocytes in bone marrow of thrombocytopenic mice", Universa Medicina, 2018 Publication	1%
3	G. YAMAOKA. "The immature platelet fraction is a useful marker for predicting the timing of platelet recovery in patients with cancer after chemotherapy and hematopoietic stem cell transplantation : PREDICTION OF PLATELET RECOVERY BY IPF", International Journal of Laboratory Hematology, 04/2010 Publication	1%
4	Laerke Walther Junggreen Have, Henrik Hasle, Else Marie Vestergaard, Mimi Kjaersgaard. "Absolute immature platelet count may predict imminent platelet recovery in thrombocytopenic	<1%

children following chemotherapy", Pediatric Blood & Cancer, 2013
Publication

5	J BLANEY. "Mutations which enhance the replication of dengue virus type 4 and an antigenic chimeric dengue virus type 2/4 vaccine candidate in Vero cells", Vaccine, 2003 Publication	<1%
6	bmchematol.biomedcentral.com Internet Source	<1%

Exclude quotes	Off	Exclude matches	< 10 words
Exclude bibliography	On		