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## PLATELET INDICES FOR PREDICTING LIVER FIBROSIS IN PATIENTS WITH CHRONIC HEPATITIS B INFECTION

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### ABSTRACT

Chronic Hepatitis B involves liver parenchymal destruction leading to fibrosis. Decreased serum thrombopoietin associated with liver cell failure is thought as the leading cause of thrombocytopenia. Mean Platelet Volume (MPV) and Platelet Distribution Width (PDW) describe platelet size and degree of variation in platelet size respectively. The researchers intended to investigate whether platelet count, MPV, and PDW were variables to determine the severity of liver fibrosis in chronic hepatitis B patients. An observational study was carried out at the Dr. Wahidin Sudirohusodo Hospital Makassar from January 2015 until December 2016. A total of 100 chronic hepatitis B patients with negative HBeAg who underwent Fibroscan and complete blood count test were included in this study. A total of 100 chronic hepatitis B patients comprising, 11 with severe liver fibrosis, 16 with moderate liver fibrosis, 46 with mild liver fibrosis, and 27 with normal liver. There were significant differences in platelet count and MPV among liver fibrosis groups with p-value <0.001 and 0.046 respectively. No significant difference was observed for PDW among liver fibrosis groups (p=0.131). This study showed that platelet count and MPV were significantly different among the normal group, mild liver fibrosis group, moderate liver fibrosis group and severe liver fibrosis group in chronic hepatitis B patients. The researchers recommend to carry out studies with larger samples in number and distributed more evenly.

**Key word:** Platelet count, MPV, PDW, fibrosis, chronic hepatitis B

### INTRODUCTION

Hepatitis B is a liver infection due to hepatitis B virus which can cause acute and chronic disease. Acute hepatitis B shows symptoms of icterus, fatigue, nausea, vomiting, and abdominal discomfort for several weeks. Chronic hepatitis B is defined as hepatitis B infection for at least six months which can lead to cirrhosis and hepatocellular carcinoma. The World Health Organization (WHO) defined cirrhosis as a diffused histopathologic changes of the liver, characterized by fibrosis and abnormal hepatic nodules. Chronic hepatitis B can persist whether with positive or negative hepatitis B envelope antigen (HBeAg). Prevalence of chronic hepatitis B with negative HBeAg keeps increasing in the last decade.<sup>1</sup>

Hepatitis B viral infection has become a global health problem in the world, including Indonesia. An estimated one-third of the world population or 240 million people are infected with hepatitis B chronically.<sup>1-3</sup> Higher prevalence is found in developing countries such as Indonesia. Hepatitis B prevalence in Indonesia is estimated as 2.5-10 %.<sup>4</sup>

Determination of fibrosis stage is needed to monitor disease progressivity. Non-invasive

modality such as ultrasound transient elastography/Fibroscan becomes the first choice in determining fibrosis stage. Fibroscan evaluates the liver stiffness (kPa) correlating with fibrosis stage.<sup>5</sup>

Thrombopoietin (TPO) is mainly produced in the liver. Thrombopoietin plays a role in megakaryocyte maturation. Liver cell damage will affect thrombopoietin production leading to decreasing platelet count. Mean platelet volume is the mean volume of circulating platelet, and it reflects the stimulation and production of platelets. An elevated MPV is associated with increasing younger and bigger platelet. Platelet distribution width describes platelet variety index quantitatively. An elevated PDW indicates a variation of platelet size and predicts the platelet activity.<sup>6,7</sup>

Ceylan *et al.* found a significant difference between severe and mild fibrosis for platelet count. Karagoz *et al.*, and Hu *et al.*, showed a higher MPV in chronic hepatitis B patients than control, while PDW was not significantly different.<sup>8-10</sup>

A study of platelet count, MPV, and PDW in different fibrosis stages of chronic hepatitis B infection with negative HBeAg as long as we know has never been held in Makassar.

This study aimed to see the difference of platelet count, MPV, and PDW among fibrosis stages of negative HBeAg chronic hepatitis B.

## METHODS

This study was a retrospective observational using secondary data of patients with chronic hepatitis B infection at the Dr. Wahidin Sudirohusodo Hospital Makassar from January 2015 until December 2016. Patients with chronic hepatitis B infection who underwent complete blood count test, other tests associated with chronic infection of hepatitis B (positive HBsAg, negative HBeAg, and positive anti-HBc) and Fibroscan were enrolled in this study. Patients were classified into four groups based on liver stiffness (kPa) which was evaluated with Fibroscan. The four groups were normal (F0), mild fibrosis (F1), moderate fibrosis (F2), and severe fibrosis with liver stiffness <5 kPa, 5-9 kPa, 9.1-14.5 kPa, and >14.5 kPa, respectively.

These research used 22<sup>nd</sup> version SPSS for data analysis. Analyzed by Kolmogorov-Smirnov test, it was found that age, platelet count and MPV were normally distributed while PDW was not normally distributed. Platelet count and MPV were displayed as mean  $\pm$  Standard Deviation (SD) while PDW was displayed as median (minimum-maximum). The difference of platelet counts and MPV were analyzed by oneway ANOVA test and PDW analyzed by Kruskal-Wallis test. Statistical significance was set at a p-value of less than 0.05.

## RESULTS AND DISCUSSION

Of the 100 chronic hepatitis B patients, 11 were severe fibrosis, 16 were moderate fibrosis, 46 were mild fibrosis, and 27 were normal.

Mostly, the patients were males (56%) in the age group 30-49 years old (50%) (Table 1). Wahyuni's study reported that the incidence of chronic liver disease was highest in 40-49 years old males. This group age is the productive age so the people have high exposure to chronic liver disease risk factors such as hepatitis virus.<sup>11</sup>

The oneway ANOVA test showed a significant difference for platelet counts in fibrosis stages of chronic hepatitis B ( $p < 0.001$ ). The least platelet count was found in severe fibrosis ( $163,300 \pm 78,200$ ) and the highest platelet count was found in mild fibrosis ( $278,500 \pm 7,820$ ). Post hoc Bonferroni test showed differences for mean platelet count between severe fibrosis, mild fibrosis ( $p < 0.001$ ), and normal ( $p = 0.001$ ). Although the researchers did not observe a significant difference between the other groups for

**Table 1.** Chronic hepatitis B samples characteristics

Characteristics		N	%
Gender	Male	56	56
	Female	44	44
Age	< 30 years	18	18
	30 -39 years	26	26
	40 -49 years	24	24
	50 -59 years	21	21
	$\geq 60$ years	11	11
Fibrosis stage	Normal	27	27
	Mild	46	46
	Moderate	16	16
	Severe	11	11

Source: Secondary data

**Table 2.** Comparison of fibrosis stages for platelet count

		n	Mean $\pm$ SD	p
Fibrosis	Normal	27	267.7 $\pm$ 56.3	< 0.001
	Mild	46	278.5 $\pm$ 78.2	
	Moderate	16	227.2 $\pm$ 59.9	
	Severe	11	168.0 $\pm$ 62.4	

Oneway ANOVA test. Post hoc Bonferroni: Severe vs Moderate  $p = 0.181$ ; Severe vs Mild  $p < 0.001$ ; Severe vs Normal  $p = 0.001$ ; Moderate vs Mild  $p = 0.069$ ; Moderate vs Normal  $p = 0.398$ ; Mild vs Normal  $p = 1.000$ .

mean platelet count (Table 2), Ceylan showed a significant difference between severe and mild fibrosis for platelet count.<sup>8</sup>

Platelet sequestration and the decrease of thrombopoietin were the main causes of thrombocytopenia. Thrombopoietin which plays a role in megakaryocyte maturation was mainly produced in the liver. Liver failure caused decrease of thrombopoietin leading to thrombocytopenia. Liver failure in mild fibrosis group was not as severe as in the severe fibrosis group so the platelet count became lower in the severe fibrosis group.<sup>8</sup>

**Table 3.** Comparison of fibrosis stages for MPV

		n	Mean $\pm$ SD	p
Fibrosis	Normal	27	9.0 $\pm$ 1.3	0.046
	Mild	46	9.1 $\pm$ 1.2	
	Moderate	16	8.7 $\pm$ 1.0	
	Severe	1	10.0 $\pm$ 1.4	

Oneway ANOVA test. Post hoc Bonferroni analysis: Severe vs. Moderate  $p = 0.044$ ; Severe vs. Mild  $p = 0.132$ ; Severe vs. Normal  $p = 0.101$ ; Moderate vs. Mild  $p = 1.000$ ; Moderate vs. Normal  $p = 1.000$ ; Mild vs. Normal  $p = 1.000$ .

The oneway ANOVA test showed a significant difference in the fibrosis group in chronic B hepatitis for MPV ( $p = 0.046$ ). The highest MPV was found in

the severe fibrosis group ( $10.0 \pm 1.4$ ), and the least was found in the moderate fibrosis group ( $8.7 \pm 1.0$ ). Post hoc Bonferroni test showed that MPV was significantly different between severe and moderate fibrosis ( $p=0.044$ ), but it was not significantly different between the other groups ( $p>0.05$ ) (Table 3). Karagoz *et al.*, and Hu *et al.*, showed a higher MPV in chronic B hepatitis than in controls.<sup>9,10</sup>

Mean platelet volume reflects mean platelet size in circulation. The platelet half-life in chronic liver disease is shorter and is associated with platelet sequestration in the spleen. Platelet production is affected by increasing interleukin-6 (IL-6) which is caused by inflammation. A shorter platelet half-life created increasing platelet production in bone marrow and releasing young platelets to the circulation which lead to elevated MPV.<sup>9,12</sup>

**Table 4.** Comparison of fibrosis stages for PDW

	n	Mean $\pm$ SD	p
Normal	27	12.1 (7.5 – 20.3)	0.131
Fibrosis Mild	46	11.4 (7.0 – 22.8)	
Moderate	16	11.7 (9.1 – 16.0)	
Severe	1	13.0 (10.5 – 16.3)	

\*Kruskal-Wallis Test

The Kruskal-Wallis test showed no significant difference for PDW in the fibrosis groups ( $p=0.131$ ) (Table 4). Karagoz *et al.* concluded that there was no significant correlation between fibrosis stages for PDW. Platelet distribution width described the variation of platelet size. Breakage of young platelets in chronic hepatitis B with severe fibrosis caused variation of platelet size leading to an elevated PDW.<sup>8,9</sup>

Ceylan *et al.* found a higher PDW in severe fibrosis than in mild fibrosis. Chronic B hepatitis with positive or negative HBeAg was included in Ceylan's study. The subjects in this study were HBeAg negative chronic hepatitis B patients with higher proportion of normal and mild fibrosis group than moderate and severe fibrosis group.<sup>8</sup>

## CONCLUSION AND SUGGESTION

This study showed a significant difference among fibrosis stages for platelet counts and MPV while no significant difference among fibrosis stages for PDW. The researchers recommend to carry out further

studies with more samples and distributed more evenly.

## REFERENCES

1. WHO. Background in guidelines for the prevention, care, and treatment of persons with chronic hepatitis B infection. Switzerland, World Health Organization, 2015; 14-24.
2. Kementrian Kesehatan RI. Situasi dan analisis hepatitis dalam pusat data dan informasi kementrian kesehatan RI. Jakarta Selatan, Kementrian Kesehatan RI, 2014; 1-6.
3. Gani AR, Hasan I, Djumhana A, Setiawan PB. Epidemiologi hepatitis B in konsensus nasional penatalaksanaan hepatitis B. Jakarta, Perhimpunan Peneliti Hati Indonesia. 2012; 1.
4. Yano Y, Utsumi T, Lusida MI, Hayashi Y. Hepatitis B virus infection in Indonesia in World Journal of Gastroenterology. California, Baishideng Publishing Group Inc. 2015; 10714-20.
5. Boesecke C, Wasmuth JC. Hepatitis B in hepatology. A clinical textbook. 3<sup>rd</sup> Ed., Germany, Flying Publishers, 2012; 34-43.
6. Wirawan R. Penilaian parameter hematologi umum dan parameter tambahan dengan alat Sysmex XE-Series. Jakarta, Fakultas Kedokteran Universitas Indonesia. 2013; 18-24.
7. Hoffman R, Benz EJ, Shattil AJ, Furie B, Cohen HJ, *et al.* Interpretation of automated blood cells analysis in hematology: Basic principles and practice. 3<sup>rd</sup> Ed., Pennsylvania, Churchill Livingstone Inc. 2000; 2470-2.
8. Ceylan B, Mete B, Fincanci M, Aslan T, Akkoyunlu Y, *et al.* A new model using platelet indices to predict liver fibrosis in patients with chronic hepatitis B infection. Central European Journal of Medicine. Springer, 2013; 453-60.
9. Karagoz E, Ulcay A, Tanoglu A, Kara M, Turhan V, *et al.* Clinical usefulness of mean platelet volume and red cell distribution width to platelet ratio for predicting the severity of hepatic fibrosis in chronic hepatitis B virus patients. European Journal of Gastroenterology and Hepatology, Lippincott Williams & Wilkins, 2014; 26(12): 1320-4.
10. Hu Y, Lou Y, Chen Y, Mao W. Evaluation of mean platelet volume in patients with hepatitis B virus infection. International Journal of Clinical Experiment in Medicine. 2014; 7(11): 4207-13.
11. Wahyuni RD. Analisis derajat fibrosis hati dengan FibroScan, indeks FIB4, King's Score dan APRI Score pada penyakit hepatitis kronis. Jurnal Kesehatan Tadulako, 2016; 2(2): 42-5.
12. Ekiz F, Yuksel O, Kocak E, Yilmaz B, Altinbas, *et al.* Mean platelet volume as a fibrosis marker in patients with chronic hepatitis B. Journal of Clinical Laboratory Analysis, 2014; 25(3): 162-5.