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CORRELATION BETWEEN ALPHA FETOPROTEIN AND PLATELET PROFILE IN HEPATOCELLULAR CARCINOMA

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ABSTRACT

Hematology abnormalities are commonly found in Hepatocellular Carcinoma (HCC) patients. Platelet (PLT) count in HCC can be low, normal or high, and influenced by tumor and liver damage. There are limited studies about the correlationp between AFP and platelet profile of HCC in Indonesia, especially in Makassar. This study is aimed to analyze the correlation between AFP and platelet profile in HCC patients. A retrospective cross-sectional study was carried out from January 2016 to June 2017 on 231 HCC subjects. The correlation between AFP and platelet profile, the correlation of AFP and platelet profile with the diagnosis were analyzed by Independent t-test and Chi-Square. There was no significant correlation between AFP and PLT profile and no significant correlation between AFP and HCC with and without cirrhosis with $p>0.05$ and $p=0.094$, respectively. Platelet count and PCT were significantly lower in cirrhotic HCC ompared to non-cirrhotic HCC ($p<0.01$, $p<0.01$, respectively), PDW and MPV were significantly higher in cirrhotic HCC compared to non-cirrhotic HCC ($p<0.05$, $p<0.05$, respectively). Mean platelet count and PCT in cirrhotic HCC were significantly lower compared to non-cirrhotic HCC, and mean PDW and MPV in cirrhotic HCC c were significantly higher compared to non-cirrhotic HCC. Further research was suggested to evaluate tumor size and nodules of HCC.

Key words: HCC, AFP, platelet profile, cirrhosis

INTRODUCTION

Hepatocellular Carcinoma (HCC) is a primary malignant liver tumor derived from hepatocytes.[1,2] The incidence of HCC is the fifth most common cancers in the world among males and the ninth among females.[1,3] The most common causes of this disease are Hepatitis B Virus (HBV) and Hepatitis C Virus (HCV).[4] This disease has highly variable clinical manifestations, from asymptomatic to symptomatic, such as pain or discomfort in the right upper quadrant of the abdomen followed by liver failure, such as malaise, anorexia, weight loss and jaundice.[5]

Moreover, HCC diagnosis is established based on the criteria of the European Association for Study of Liver Congress, such as focal lesions > 2 cm with arterial hypervascularization (using Abdominal Ultrasound Imaging, Computed Tomography Scan, or Magnetic Resonance Imaging) and high levels of serum AFP.[6] Alpha-fetoprotein (AFP) is a normal serum protein mostly synthesized by fetal liver cells and yolk-sac cells. In addition, a little amount of AFP is also synthesized by the fetal gastrointestinal tract. The normal range of serum AFP is 0-20 ng/mL, while in HCC patients it increases from 60% to 70%, and AFP level > 400 ng/mL can be used to indicate HCC.[7]

Moreover, hematological abnormalities are often found in HCC patients.[8,9] Tumor and liver damage can lead to decreased, normal, or increased platelet count in HCC. After the stage of cirrhosis, patients with hepatocellular carcinoma will undergo liver decompensation, liver failure, and portal hypertension. Therefore, the decreased platelet count was frequently reported. In addition, the size of nodules in HCC patients with cirrhosis is usually small since the development of HCC nodules is inhibited by liver parenchymal damage. Patients with non-cirrhotic Hepatocellular carcinoma (NC-HCC), on the other hand, will have high platelet counts and large tumor size since nodules can develop with minimal liver damage and high alpha-fetoprotein level.[10,11]

Unfortunately, theare still limited number of studies to determine the significance of PDW, MPV and PCT values in HCC patients. Kurt *et al*. have already found that MPV value was significantly higher in HCC patients than non-HCC patients, thus, MPV value can be used as a diagnostic marker in HCC.[12] However, there is still no research on the correlation between AFP and platelet profiles in HCC patients in Indonesia, especially in Makassar. Hence,

this research aimed to determine the correlation between AFP and platelet profiles in HCC patients.

METHODS

This research was carried out at the Installation of Clinical Pathology Laboratory and Medical Record of the Dr. Wahidin Sudirohusodo General Hospital in Makassar from August 2017 until sufficient number of samples were obtained. The research used a cross-sectional design with a retrospective approach. The inclusion criteria for the research samples were all medical record data of patients with diagnosis of HCC based on the results of laboratory tests and radiology imaging at the Dr. Wahidin Sudirohusodo General Hospital in Makassar from January 2016 to June 2017.

The results of this research were statistically analyzed using SPSS version 22, descriptive statistics, and statistical tests. The correlation between AFP and platelet profiles was then determined using independent t-test and Chi-Square, p-value <0.05 suggested significant results.

This research has been approved by the Health Research Ethics Committee of University of Hassanudin/Dr. Wahidin Sudirohusodo General Hospital No 555/H4.8.4.5.31/PP36-KOMETIK/2017.

RESULTS AND DISCUSSION

This research was performed at the Dr. Wahidin Sudirohusodo General Hospital in Makassar. This research used medical record data from January 2016 to June 2017. 231 patients with a diagnosis of HCC were involved as the research subjects. The characteristics of those research subjects can be seen in Table 1.

Research subjects were predominantly male patients with sex ratio of 3: 1. It was also known that the research subjects were mostly from the age group of 60-69 years old. The general incidence of HCC in some countries is twice higher in males than in females. The highest number of its incidence was found in East and Southeast Asia. This was associated with the high prevalence of hepatitis virus infection in those areas. Furthermore, the incidence of HCC was more commonly found in old age since HBV infection was considered as one of the most important causes of HCC that requires two to three decades to develop HCC.[1] Similarly, Vnook *et al*. also found that the incidence of HCC was higher in males at older ages.[13]

There was no significant correlation between AFP profile and platelet count (p> 0.05) as illustrated in

Table 1. Characteristics of the research subjects

Variables	n (%)	Minimum	Maximum	Median	Mean	SD
Sex						
Male	173 (74.9)					
Female	58 (25.1)					
Age (years old)						
<30	4 (1.7)					
30-39	29 (12.6)					
40-49	50 (21.6)					
50-59	60 (26.0)					
60-69	65 (28.1)					
>=70	23 (10.0)					
AFP						
High increase*	180 (77.9)					
Slight increased*	51 (22.1)					
Platelets index						
Platelet		34,000	820,000	230,000	256,630	146,740
PDW		7.70	22.00	12.30	12.83	2.92
MPV		0.10	13.40	9.00	9.09	1.63
PCT		0.01	0.56	0.20	0.22	0.11
Diagnosis						
NC-HCC	159 (68.8)					
C-HCC	72 (31.2)					

Note: * AFP levels increased with significance ≥ 200 ng/mL and increased with insignificance <200 ng/mL.

Table 2. Correlation between AFP and platelet profiles

Profiles Platelet	AFP	n	Minimum	Maximum	Median	Mean	SD	p*
Platelet	High increase	180	34	819	227.00	252.86	137.78	0.464
count	Slight increase	51	40	820	253.00	269.94	175.67	
PDW	High increase	180	8.30	22.00	12.80	12.94	2.91	0.267
	Slight increase	51	7.70	21.00	12.00	12.43	2.95	
MPV	High increase	180	6.50	13.40	9.00	9.15	1.37	0.391
	Slight increase	51	0.10	12.70	8.70	8.86	2.33	
PCT	High increase	180	0.01	0.56	0.20	0.22	0.11	0.835
	Slight increase	51	0.01	0.54	0.20	0.21	0.12	

Note: * AFP levels increased with significance ≥ 200 ng/mL and increased with insignificance <200 ng/mL. * Independent t-test.

Table 3. Correlation between AFP profile and HCC diagnosis

			Diagnosis		p*
			HCC without cirrhosis	HCC with cirrhosis	
AFP	High increase	n	119	61	0.094
		%	74.8%	84.7%	
	Low increase	n	40	11	
		%	25.2%	15.3%	
Total		n	159	72	
		%	100.0%	100.0%	

Note: * AFP levels increased with significance ≥ 200 ng/mL and increased with insignificance <200 ng/mL. *Chi-Square test

Table 4. Correlation between platelet profile and HCC diagnosis

Variables	Diagnosis	N	Minimum	Maximum	Median	Mean	SD	p*
Platelet count	NC-HCC	159	34	820	255.00	280.85	148.24	0.00
	C-HCC	72	40	819	187.00	203.15	128.98	0
PDW	NC-HCC	159	7.70	22.00	12.00	12.54	2.88	0.02
	C-HCC	72	8.30	20.50	13.00	13.48	2.91	3
MPV	NC-HCC	159	.10	13.40	9.00	8.90	1.59	0.01
	C-HCC	72	6.70	13.40	9.50	9.49	1.64	1
PCT	NC-HCC	159	0.01	0.56	0.20	0.23	0.11	0.00
	C-HCC	72	0.01	0.54	0.20	0.18	0.10	1

* Independent t-test

Table 2. There was also no significant correlation between AFP and PDW profiles (p> 0.05) and no significant correlation between AFP and MPV profiles (p> 0.05). Similarly, there was also no significant correlation between AFP and PCT profiles (p> 0.05). Unlike these results, a previous research by Serag *et al*. found that high AFP value and low platelet count were significantly correlated to liver damage. Nevertheless, Serag *et al.* did not include the HCC criteria for their research subjects.[14]

There was no significant correlation between AFP value and the presence or absence of cirrhosis in HCC patients (p=0.094) as in Table 3. Unlike these results, Rino *et al*. revealed that the AFP value in C-HCC patients was higher than in NC-HCC patients.[15] However, Arrieta *et al.* found that AFP value in NC-HCC patients was higher than in C-HCC patients.[16] Alpha-fetoprotein level as a tumor marker is more associated with the size of the tumor and the number of nodules in HCC patients.

The platelet count in C-HCC patients was significantly lower than in NC-HCC patients (p <0.001) as shown in Table 4. The PDW value in C-HCC patients was also significantly higher than in NC-HCC patients (p <0.05). Furthermore, the MPV value was significantly higher in C-HCC patients than in NC-HCC patients (p <0.05). However, the PCT value was significantly lower in C-HCC patients than NC-HCC patients (p <0.01). Similar to these results, a research by Kurt *et al.* revealed that platelet count

was lower in CHCC patients because of a decrease of thrombopoietin production and platelet sequestration due to splenomegaly in those patients.[17]

A high MPV value is generally associated with a highly inflammatory process. High MPV indicates great platelet count circulating in the blood. Generally, MPV increases in chronic diseases. Kurt *et al*. even found that MPV was considered as a potential marker of HCC in patients with chronic liver disease.[17] Fewer platelet counts, as the result, can trigger release of immature platelets into the circulation and increase MPV values. PDW value as an indicator of variability of platelet volume will also increase in platelet an isocytosis. Consequently, correlation between PDW and MPV was found in this research. PCT, on the other hand, is platelet expressed as a percentage of total blood volume. Therefore, low PCT and low platelet count can indicate a large platelet consumption in C-HCC patients.[18]

CONCLUSION AND SUGGESTION

There was no correlation between AFP levels and platelet profiles in HCC. The mean of platelet count and PCT in C-HCC patients were significantly lower than in NC-HCC patients. The mean values of PDW and MPV in cirrhotic HCC patients were significantly higher than in non-cirrhotic HCC patients. As the result, further studies were needed to evaluate the size of the tumor and the number of nodules in HCC patients.

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