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The Analysis of MPV, Plateletcrit, Platelet Distribution Width, and Total Platelets in AKI

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ABSTRACT

Patients with Acute Kidney Injury (AKI) who require hemodialysis had been reported to have a mortality rate of 50-70% in the last 30 years. Platelet and platelet index are two of the important hematological markers to be analyzed in AKI. This study aimed to analyze the levels of MPV, PCT, PDW, and total platelets in patients with AKI. A retrospective study using medical record data of 122 patients with AKI from January 2019 to December 2020 was conducted in Dr. Wahidin Sudirohusodo Hospital, Makassar. Patients were grouped based on disease outcomes and consisted of patients who died in the hospital and patients who recovered. Measurement of MPV, PCT, PDW, and platelet count was performed using a hematology analyzer. Mann-Whitney and independent T-tests were used for statistical analysis. The subjects of this study consisted of 80 AKI patients who died and 42 who recovered, the most affected age was ≥ 56 years old. The mean MPV was significantly higher in subjects who died in the hospital (10.31±1.53 fL) than in patients who recovered (9.5±1.39 fL) ($p<0.01$). Mean PCT was higher in subjects who died in the hospital (0.85%) than in patients who recovered (0.18%), despite statistical insignificance ($p>0.05$). Mean PDW was higher in subjects who died in the hospital (14.2 fL) than in patients who recovered (13.2 fL), despite statistical insignificance ($p>0.05$). Mean platelet was lower in subjects who died in the hospital (174.3 $x10^9$L) than in patients who recovered (215.6 $x10^9$L), despite statistical insignificance ($p>0.05$). Mean platelet volume levels were elevated in AKI patients with poor outcomes, possibly associated with the pathogenesis of more severe inflammation caused by hyperaggregation and peripheral destruction of platelets, which provide positive feedback to the bone marrow to produce larger and more active platelets. The MPV levels were significantly higher in AKI patients with poor outcomes, whereas PCT, PDW, and total platelet levels were not significant.

Keywords: Mean platelet volume, PCT, PDW, platelets, acute kidney injury

INTRODUCTION

The Acute Kidney Injury Network (AKIN) defines Acute Kidney Injury (AKI) as a functional and structural disorder or the presence of signs of kidney damage, which include abnormalities in blood and urine tests or tissue morphology, which occur in less than 3 months.[1]

The diagnosis of AKI according to the Kidney Disease Improving Global Outcome (KDIGO) is an increase in serum creatinine (Scr) ≥ 0.3 mg/dL (≥ 26.5 μmol/L) within 48 hours or an increase in serum creatinine ≥ 1.5 times compared to the initial value, which occurs within 7 days or urine volume <0.5 mL/kg/hour for 6 hours.[1,2]

Research on the incidence of AKI in the world states that 20% of patients who are hospitalized have AKI. Studies in Asia show that the incidence of AKI is 19.4% in East Asia; 7.5% in South Asia; 31.0% in Southeast Asia; 9.0% in Central Asia and 16.7% in West Asia. Meanwhile, it was reported that the mortality of AKI was 36.9% in East Asia, 13.8% in South Asia, and 23.6% in West Asia. There were 586 cases of AKI with hospitalization at Dr. Wahidin Sudirohusodo Hospital in 2020. Patients with AKI who require hemodialysis had been reported to have a mortality rate of 50-70% and remained constant over the last 30 years.[2,3]

The etiology of AKI is generally divided into pre-renal, renal, and post-renal. The pathophysiology of AKI includes complex disorders of vascular, tubular, inflammatory factors, and other factors such as hemodynamic disturbances, infections, and toxins. If AKI continues, it will be followed by the formation of fibrosis which ends in Chronic Kidney Disease (CKD).[3]

There are several criteria used to help diagnose AKI. One of the criteria used is the RIFLE criteria (risk, injury, failure, loss, end-stage kidney disease).[4]

To date, no specific therapy can treat AKI, resulting in urgency in early recognition and management. Early recognition of patients at risk for AKI can produce better outcomes compared to therapy for an established diagnosis of AKI. [3]

Platelets are the first cells to arrive at the site of acute injury where they interact with endothelial cells and leukocytes. Under physiological conditions, in which the endothelium remains physically and biochemically intact, circulating platelets are in an inactive state. However, endothelial cell function changes in AKI, leading to reduced antiplatelet regulation and platelets are exposed to activating factors. Platelets also facilitate inflammation during the pathophysiology of AKI, primarily because they can stimulate endothelial cells and recruit and activate leukocytes during inflammatory reactions.[5,6]

Preliminary data from animal and human studies and randomized clinical trials suggest that antiplatelet therapy reduces the risk of AKI. Linden *et al.* reported that thrombocytopenia increases the risk of AKI after aortic valve implantation, and is an important risk factor for postoperative AKI. Miklos *et al.* found that the lowest platelet count after coronary artery bypass grafting was significantly associated with postoperative AKI. Wu *et al*., and Sunusi *et al.* also found that platelet count can be a useful biomarker for the incidence of AKI in hemorrhagic and non-hemorrhagic strokes.[6-9]

A platelet index is a group of parameters used to assess the size, morphology, and kinetic proliferation of platelets. Platelet indices such as the Mean Platelet Volume (MPV), plateletcrit (PCT), and Platelet Distribution Width (PDW) are easily calculated through routine blood counts. Compared to other platelet indices, the MPV and PDW are platelet indices that are better known as indicators and markers of platelet activation.[10,11]

There has been no data on research, which discusses platelet analysis and platelet index in AKI patients in Indonesia. This study compared MPV, PCT, PDW, and total platelet levels in AKI patients concerning the outcome of death and recovery.

Based on the background above, the authors would like to perform a study on the analysis of MPV, PCT, PDW, and total platelets in patients with AKI.

METHODS

A retrospective study was carried out using secondary data from medical records of patients diagnosed with AKI and undergoing hospitalization at Dr. Wahidin Sudirohusodo Hospital from January 2019 to December 2020. The study population was all patients aged >18 years with a clinical diagnosis of AKI at Dr. Wahidin Sudirohusodo Hospital whose results were of the Complete Blood Count (CBC) test. Patients with a history of platelet transfusion, diagnosis of immune thrombocytopenic purpura, dengue hemorrhagic fever, and CKD were excluded from this study.

The parameters used in this study were MPV, PCT, PDW, and total platelet count based on the test results using a hematology analyzer.

Data were statistically analyzed using SPSS version 25. Descriptive statistical calculations and frequency distribution were used for statistical analysis. In addition to the Kolmogorov-Smirnov test used to determine data normality, the Chi-Square test, the independent T-test, and the Mann-Whitney test were also used. The statistical test result with a p-value <0.05 was reported as significant.

Ethical eligibility approval was obtained from the Health Research Ethics Commission (KEPK) Faculty of Medicine, Hasanuddin University/Dr. Wahidin Sudirohusodo Hospital, Makassar with number: 21503/UN4.6.8/PT.01.04/2021.

RESULTS AND DISCUSSIONS

The research was performed at the Medical Record Installation of Wahidin Sudirohusodo Hospital in October 2020 involving a total population of 926 patients, which resulted in a total of 122 patients with AKI who met the inclusion criteria. The characteristics of the research sample can be seen in Table 1.

Table 1 shows that most of the subjects were male (66.4%), the highest age range was 56-65 years (36.1%) and ≥ 65 years (27.9%), and the highest number of outcomes was death found in 80 subjects (65.6%). The mean age of the patients who participated in this study was 58.17±14.66 years. Platelet values (x109L) varied between 15–1.071 with a mean value of 188.48±141.54. MPV values (fl) varied from 6.9 to 14.3 with a mean value of 10.03±1.53. The PCT value (%) varied between 0.01 and 27.3 with a mean value of 0.62±2.80. The PDW value (%) varied from 7.4 to 29.8 with a mean value of 13.86±3.76. The data of age, MPV, and PDW were normally distributed (all with p>0.05), whereas data of total platelets and PCT were not normally distributed (all with p<0.001).

Table 2 shows that the percentage of death in female patients was higher (71%) compared to that of male patients (63%), despite statistical insignificance (p>0.05). The highest percentage of death was found at the age of 45-55 years (76%) and the lowest was found at the age of 18-35 years (44%), despite statistical insignificance (p>0.05).

Table 1. Characteristics of research subjects (n=122)

Variable	n	(%)	Min	Max	(Mean)	SD	p*
Gender							
Male	81	66.4					
Female	41	33.6					
Total	122	100.0					
Age group**			18	89	58.17	14.66	0.026
18-35 years	9	7.4					
36-45 years	10	8.2					
46-55 years	25	20.5					
56-65 years	44	36.1					
≥ 65 years	34	27.9					
Total	122	100.0					
Outcome							
Death	80	65.6					
Recovery	42	34.4					
Total	122	100.0					
Platelet (x10^9L)			15	1071	188.48	141.54	<0.001
MPV (fL)			6.9	14.3	10.03	1.53	0.200
PCT (%)			0.01	27.3	0.62	2.80	<0.001
PDW (fL)			7.4	29.8	13.86	3.76	0.054

*Kolmogorov-Smirnov test, **Age group according to the Ministry of Health

Table 2. Distribution of outcome according to gender and age **

		Outcome		
Gender		Death	Recovery	Total
Male	n	51	30	81
	%	63.0%	37.0%	100.0%
Female	n	29	12	41
	%	70.7%	29.3%	100.0%
Total	n	80	42	122
	%	65.6%	34.4%	100.0%
Age group				
18-35 years	n	4	5	9
	%	44.4%	55.6%	100.0%
36-45 years	n	5	5	10
	%	50.0%	50.0%	100.0%
46-55 years	n	19	6	25
	%	76.0%	24.0%	100.0%
56-65 years	n	29	15	44
	%	65.9%	34.1%	100.0%
>65 years	n	23	11	34
	%	67.6%	32.4%	100.0%
Total	n	80	42	122
	%	65.6%	34.4%	100.0%

*Chi-Square test (p=0.394) **Chi-Square test (p=0.389)

The platelet analysis and platelet index according to the outcome can be seen in Table 3.

Table 3 shows that the mean MPV was significantly higher in subjects who died (10.31±1.53 fL) than in those who recovered (9.5±1.39 fL) (p<0.01). The mean PCT was found to be higher in subjects who died (0.85%) than in those who did not die (0.18%), despite statistical insignificance (p>0.05). The mean PDW was found to be higher in subjects who died (14.2 fL) than in those

Table 3. Analysis of MPV, PCT, PDW, and platelet count

		Outcome		
Variable	Statistic	Death (n=80)	Recovery (n=42)	p
Platelet (x1000)	Minimum	15	45	0.074*
	Maximum	1071	650	
	Median	147.50	197.50	
	Mean	174.26	215.55	
	Standard Deviation	139.99	142.19	
MPV	Minimum	7.2	6.9	0.005**
	Maximum	14.3	11.9	
	Median	10.20	9.65	
	Mean	10.31	9.51	
	Standard Deviation	1.53	1.39	
PCT	Minimum	0.01	0.04	0.366*
	Maximum	27.30	0.50	
	Median	0.19	0.19	
	Mean	0.85	0.18	
	Deviation	3.45	0.10	
PDW	Minimum	7.4	8.1	0.176**
	Maximum	29.8	20.8	
	Median	13.40	13.20	
	Mean	14.19	13.22	
	Standard Deviation	4.13	2.86	

*Mann-Whitney test **Independent T-test

who did not die (13.2 fL), despite statistical insignificance (p>0.05). The mean total platelets were lower in subjects who died (174.3 x10^9) than in those who did not die (215.6 x10^9), despite statistical insignificance (p>0.05).

ROC curve analysis was used to determine the MPV cut-off value as shown in Figure 1.

The ROC curve for the MPV parameter in Figure 1 shows an Area Under Curve (AUC) value of 0.640 or 64%. Based on the coordinate levels of the ROC curve, a cut-off value of 8.8 fL was obtained with a sensitivity of 83.8% and a specificity of 38.1%.

Based on the results of the study in Table 1, it was found that the research subjects were patients aged 18-89 years with the highest age range of 56-65 years (36.1%) and ≥ 65 years (27.9%). This was in accordance with the research of Cong *et al.*, which suggested that age is an independent risk factor for AKI, which may be caused by renal atherosclerosis and decreased kidney capacity in elderly patients. Almost all studies related to this matter state that decreased kidney function is a very important risk factor for AKI.[12,13]

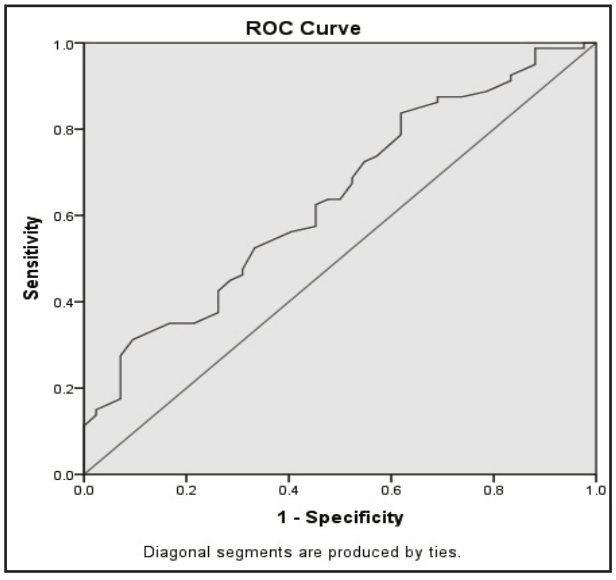

Figure 1. ROC curve

Based on the results of the study in Table 2, it was found that the percentage of subjects who died was higher in patients aged 45-55 years (76%) compared to older age. A study by Xu *et al.* concluded that although more elderly AKI patients die in hospitals,

elderly patients do not have a higher mortality risk than younger AKI patients. The insignificant results we found might probably be due to the insufficient number of samples.[14]

Based on the results of the study in Table 3, it was found that the MPV value was significantly higher in AKI patients with poor/dead outcomes compared to AKI patients who improved/recovered ($p<0.01$). This was in accordance with a study by Han *et al*., which found that an increased MPV value in critically ill patients could indicate more severe inflammation and might be related to hyperaggregatability and peripheral damage/increased platelet activity. This condition will provide positive feedback to the bone marrow to produce larger and more active platelets. Table 3 also shows that the total platelet count was not significantly different between AKI patients who died and those who recovered. This was in line with a study from Han *et al*. suggesting that a single measurement of the platelet count is not sufficient to represent the patient's prognosis because thrombocytopenia in critically ill patients in the ICU is considered a poor prognostic marker. The MPV value is a significant prognostic marker in AKI patients who require hemodialysis. Another study by Li *et al*. also stated the same thing.[14]

Platelet distribution width directly measures variability in platelet size, and changes in platelet activation, and indicates heterogeneity in platelet morphology. In this study, the mean PDW was higher in AKI patients who died than those who recovered/improved, although the difference was not statistically significant. These results were in line with a study by Young *et al*., which reported that the increase in PDW was proportional to the decrease in the estimated Glomerular Filtration Rate (eGFR).[15]

The mean PCT in this study was higher in AKI patients who died than those who recovered/improved, although the difference was not statistically significant. However, these results were in contrast to other studies by Emara *et al*. and Gao *et al*., which found a tendency for lower PCT levels in AKI patients. However, this study had limited data, which caused difficulty to avoid bias in medical record data.[16-18]

CONCLUSIONS AND SUGGESTIONS

Mean platelet volume levels in AKI patients with poor outcomes were significantly higher than in AKI patients with good outcomes ($p<0.01$); MPV levels at a cut-off of ≥ 8.8 fL could predict a worse outcome for AKI patients. PCT, PDW, and total platelet levels were not significant in AKI patients with poor outcomes compared to AKI patients with good outcomes, despite statistical insignificance ($p>0.05$).

Mean platelet volume levels are recommended to be observed in patients with AKI to monitor therapy and predict outcomes.

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