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Analysis of Urea, Creatinine, and Platelet Indices in Hypertensive Patients

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ABSTRACT

Hypertension may lead to complications of kidneys and blood vessels. Measurement of urea, creatinine, and platelet indices can be markers of renal function and endothelial dysfunction in hypertensive patients. This study aimed to analyze the profile and correlation between renal function parameters such as urea and creatinine and platelet indices (MPV, PDW, and PCT) with blood pressure in hypertensive patients. One hundred and thirty-third hypertensive patients treated at Wahidin Sudirohusodo Hospital from April to July 2019 were involved in this cross-sectional study. Researchers collected demographic data, blood pressure degrees (based on ESC 2018), systolic and diastolic blood pressure, and urea, creatinine, and platelet index value (MPV, PDW, and PCT) data from the medical record. Descriptive analysis, Spearman test, Fisher exact test, and Kruskal-Wallis test were used confidence interval of 95%. A total of 133 participants were involved in this research. There were significant difference between the mean age (p=0.023), MPV (p=0.032), and PCT (p=0.019) to the degree of hypertension, while gender (p=0.185), urea (p=0.106), creatinine (p=0.498), platelet (p=0.094) and PDW (0.826) showed no significant difference. The bivariate correlation test showed that urea (rs= -0.232 p=0.007) and creatinine (rs= -0.180 p=0.038) had a positive correlation with systolic blood pressure. Platelets index, MPV (rs=0.285 p=0.001), and PDW (rs=0.179) were positively correlated to systolic blood pressure. Also, urea levels and creatinine were positively correlated with MPV value. There was an increase in MPV along with the increase of urea, creatinine. An increase in MPV could be a predictor of endothelial damage and the risk of atherothrombosis.

Keywords: Hypertensive, urea, creatinine, platelet indices

INTRODUCTION

Hypertension is a major health problem worldwide with a high prevalence rate. Hypertension is a clinical manifestation of hemodynamic balance disorders of the cardiovascular system with multi-factor etiology.[1] Hypertension is a clinical condition in which a person's blood pressure is higher than normal, with systolic blood pressure ≥ 140 mmHg and diastolic blood pressure ≥ 90 mmHg. European Society of Hypertension (ESH) 2018 further classifies hypertension into: Grade 1 (TDS 140-159 mmHg and/or TDD 90-99 mmHg), Grade 2 (TDS 160-179 mmHg and/or TDD 100-109 mmHg), and Grade 3 (TDS ≥ 180 mmHg and or TDD ≥140 mmHg).[2,3]

The prevalence of hypertensive patients continues to increase. Data from the World Health Organization (WHO) in 2015 showed that about 1.13 billion people in the world suffer from hypertension (1 in 4 males and 1 in 5 females).[1] The National Health and Nutrition Examination Survey (NHANES) from 2015 to 2016 showed that the prevalence of hypertensive patients in American adults was 29%, comprising 30.2% male and 27.7% female patients.[2] Based on the Basic Health Research (RISKESDA) survey in 2018, the prevalence of hypertension in Indonesia was 34.1%, indicating an increase compared with data in 2013, which showed only 28.2%.[4]

Hypertension is known as the killer disease and the heterogeneous group of disease because its complication can affect various target organs such as the heart, brain, kidneys, eyes, and peripheral blood vessels. Damage to these organs depends on the degree of hypertension and the length of hypertension without control and treatment.[1] Disruption of kidney function in hypertension can occur both pre-renal and renal. Vasoconstriction occurs in hypertension and decreases/reduced blood flow to the kidneys, leading to decreased Glomerular Filtration Rate (GFR) affected excretion of urea and creatinine. Also, there are changes in the parenchyma of the renal organs, glomerular

enlargement followed by damage to endothelial cells and loss of glomerular endothelial penetration (glomerular capillary endotheliosis).[5-9]

The endothelial damage that occurs induces platelet aggregation, contributing to thrombus formation, which can lead to atherothrombosis. Platelet size, measured as Mean Platelet Volume (MPV), is an indicator of platelet activity. More giant platelets have more significant prothrombotic potential, enzymatic and metabolic activity.[10,11]

Mean platelet volume, Platelet Distribution Width (PDW), and Plateletcrit (PCT) are platelet indices that are very easy to obtain on routine blood tests. Mean platelet volume is a measure of the average platelet count in the blood. Platelet distribution width is the degree of heterogeneity in platelet size.[11,12] Plateletcrit is a product of MPV, and the total number of platelets can be used as an indication of the number of platelets circulating in the blood. Research by Surgit *et al*. reported that MPV could be used as an indicator of increased platelet activity, which can be at risk of atherothrombosis in hypertensive patients.[10,12] Large platelets are associated with denser and more reactive granules. Platelet granules contain procoagulants with atherogenic potential. Platelet granules also contain Platelet-Derived Growth Factor (PDGF) and associated Vascular Endothelial Growth Factor (VEGF), which play a role in thrombus formation. There is a hypothesis that MPV is associated with an increased risk of atherothrombosis in hypertension. Platelet activation will also cause morphological changes and the construction of pseudopods; therefore, size varies and PDW increases.[10,13]

Several studies by Basant *et al.* showed an increase in urea and creatinine levels in hypertensive patients. Research by Ozgur Surgit *et al.* in Turkey showed a rise in MPV value in hypertensive patients could predict atherothrombosis risk.[6,10] This study aimed to investigate the relationship between blood pressure and complications on decreased kidney function and the tendency of atherothrombosis in hypertensive patients through analysis of urea, creatinine, PCT, MPV, and PDW levels.

METHODS

This research was a descriptive-analytical study with the cross-sectional method by taking secondary data of patients diagnosed with hypertension at the Hypertension Kidney Outpatient Clinic of Dr. Wahidin Sudirohusodo Hospital Makassar in the period of April-June 2019.

The study population was all patients diagnosed with hypertension at Dr. Wahidin Sudirohusodo Hospital, Makassar. The study sample was all patients diagnosed with hypertension and ≥ 18 years who had medical records and laboratory examinations of urea, creatinine, and complete blood at Dr. Wahidin Sudirohusodo Hospital, Makassar, from April to June 2019. Hypertension was classified based on the SH classification 2018 into Grades 1, 2, and 3. The inclusion criteria were all hypertensive patients who had routine blood tests, urea, and creatinine in their medical records. Exclusion criteria were patients with hematologic malignancies, infectious diseases, autoimmune diseases, patients undergoing hemodialysis, chemotherapy, patients receiving antithrombotic therapy, and those who suffered from coagulation disorders.

Blood tests were performed using an automated hematology analyzer with the flow cytometry method, while urea and creatinine levels were measured using a photometer method and chemistry analyzer. The data were processed using the Statistical Package for the Social Sciences (SPSS). Descriptive analysis, Spearman test, Fisher exact test, and Kruskal-Wallis test were carried out with a confidence level of 95%.

Research permission was obtained from the Health Research Ethics Committee, Faculty of Medicine of Hasanuddin University/Dr. Wahidin Sudirohusoso Hospital with number of 568/UN4.6.4.5.31/PP36/2019.

RESULTS AND DISCUSSIONS

This research was conducted from June to July 2019 by taking data from patients' medical records at Dr. Wahidin Sudirohusodo Hospital, Makassar. This study used a descriptive-analytic study design involving 133 patients who met the inclusion and exclusion criteria.

Sample characteristics were grouped based on age, gender, degree of hypertension, levels of urea, creatinine, platelets, MPV, PDW, PCT (Table 1).

Table 2 shows a significant difference in age, MPV, and PCT to the degree of hypertension, while no significant difference was found in other variables.

Table 3 shows that urea and creatinine were positively correlated with systolic but negatively correlated with diastolic blood pressure. Also, MPV and PDW were positively correlated with systolic blood pressure. Plateletcrit, however, was negatively correlated with diastolic blood pressure.

Table 1. Characteristics of research samples (n=133)

Variable	Minimum	Maximum	Mean±SD
Age (years)	18	82	55.62±1.32
Cystolic (mmHg)	100	190	147,99±13.18
Diastolic (mmHg)	65	117	83.77±19.98
Urea (mg/dL)	10	269	60.21±5.11
Creatinine (mg/dL)	0.4	13.7	2.19±2.06
Platelets (uL)	200,000	689,000	283,47±117,040
MPV (fL)	6.5	15.3	9.01±1.39
PDW (fL)	7.3	21	12.27±2.67
PCT (%)	0.01	0.60	0.14±0.13

Note: SD: Standard Deviation

Table 2. Difference of mean variables based on the degree of hypertension (n=133)

Variable	Degree of Hypertension				p-value
	Controlled (n=11) Mean±SD	Grade 1 (n=91) Mean±SD	Grade 2 (n=25) Mean±SD	Grade 3 (n=6) Mean±SD	
Age (years)[a]	49.27±13.41	58.13±12.39	51.2±14.67	55.76±15.68	**0.023***
Gender[b]					
Male	5	44	18	3	
Female	6	47	7	3	
Systolic blood pressure (mmHg)	127.6±9.80	145,0±5.44	161,5±17.2	143,1±19.3	
Diastolic blood pressure (mmHg)	78.1±7.08	80.51±9.01	90.9±11.5	86.64±11.81	
Urea (mg/dL)[a]	37.5±35.60	63.9±51.65	58.4±56.95	93.41±35.60	0.106
Creatinine (mg/dL)[a]	1.47±1.31	2.11±1.79	2.72±2.81	2.56±0.84	0.498
Platelets (uL)[a]	302,63±105,5	268,35±112,8	309.2±128.3	370,67±1.17	0.094
MPV(fL)[a]	7.92±1.09	9.12±1.35	9.09±1.60	8.95±0.82	**0.032***
PDW(fL)[a]	11.59±1.71	12.33±2.96	12.15±1.61	13.13±3.31	0.826
PCT(%)[a]	0.26±0.08	0.13±0.12	0.14±0.13	0.11±0.14	**0.019***

Note: * Significant, p-value < 0.05 a: Kruskal-Wallis test b: Fisher exact test

Table 3. Correlation test between each variable, systolic and diastolic blood pressure

Variable	Systolic	p-value	Diastolic	p-value
Age[a]	0.015	0.862	-0.118	0.176
Urea[a]	0.066	0.454	-0.232	**0.007**
Creatinine	0.016	0.858	-0.180	**0.038**
Platelets[b]	-0.072	0.412	0.236	**0.006**
MPV[a]	0.285	**0.001**	0.011	0.902
PDW	0.179	**0.040**	0.046	0.595
PC	-0.182	**0.036**	0.010	0.908

Note : a. Spearman test, b. Pearson test, p < 0.05, was significant

Correlation test results in Table 4 show a weak correlation between urea, creatinine, MPV, PDW, and PCT.

The results showed that most hypertensive patients at Dr. Wahidin Sudirohusodo Hospital suffered at the average age of 55.62±1.32 years, indicating accordance with the references stating that blood elasticity vessels begin to decrease in older age as a result of which blood pressure increases.[1]

In this study, 70 male and 63 female patients suffered from hypertension, indicating in accordance with demographic data by WHO and NHANES, which states that the prevalence of hypertension in males is higher than in females.[1,2]

Table 4. Correlation test between urea and creatinine with platelet indices

	MPV (fL)	PDW (fL)	PCT (%)
Urea (mg/dL)	r : 0.228	r : 0.107	r : 0.130
n = 133	**p : 0.008***	p : 0.218	p : 0.137
Creatinine (mg/dL)	r : 0.195	r : 0.095	r : 0.138
n = 133	**p : 0.024***	p : 0.278	p : 0.113

* Spearman correlation test, p- value < 0.05 was significant, r close to -1 or +1 showed strong correlation between two variables

The mean urea and creatinine levels in this study were 60.21±5.11 mg/dL and 2.19±2.06 mg/dL, indicating a tendency of increased urea and creatinine levels in hypertensive patients. A higher degree of hypertension led to higher urea and creatinine levels, which indicate a decreased renal function in hypertensive patients. There was no significant difference in urea and creatinine with p=0.106 and 0.498, respectively. This study's results were not in line with the research by Joshi *et al*., which showed a significant increase in urea creatinine levels in hypertensive patients with a p-value < 0.001. This irrelevant result might be caused by the uneven distribution of the sample in each hypertension degree classification.[6] From the correlation test results between systolic and diastolic blood pressure with urea and creatinine, it was shown that urea and creatinine were positively correlated with systolic blood pressure, which means that a higher systolic blood pressure led to higher serum urea and creatinine levels.

This study found that the mean of MPV, PDW, and PCT was 9.01±1.39 fL, 9.01±2.67 fL, and 0.14±0.14%, respectively. These results were within the normal range of the test at each degree of hypertension. There was a significant difference in MPV and PCT values in each hypertension degree with p=0.032 and 0.019, respectively. Correlation test showed that MPV and PDW were positively correlated with systolic and diastolic blood pressure, indicating that an increase in MPV and PDW values was in line with increased blood pressure. This result was in line with a study by Surgit *et al*., which states that increased MPV levels in hypertensive patients can be an indicator of an increased platelet activity, which can increase the risk of atherothrombosis.[10]

The correlation test between urea, creatinine, and MPV values showed a significant correlation with p=0.008 and p=0.024, indicating that urea and creatinine levels were in line with the increase in the MPV value. This showed that the declined renal function in hypertensive patients is in line with the damage to blood vessel endothelium due to vasoconstriction of blood vessels in hypertensive patients.

CONCLUSIONS AND SUGGESTIONS

There was a tendency for increased urea and creatinine levels along with increased blood pressure. Platelet index, such as MPV and PCT, rose along with increased blood pressure, while no significant difference was found in PDW at any degree of hypertension. Increased urea and creatinine levels were in line with the increased MPV. Urea, creatinine, platelet index (MPV) can be recommended for control tests in hypertensive patients.

It was suggested that hypertensive patients' old data could be considered a factor that can affect the correlation test results of the measured parameters.

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