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ARTICLE

MEAN PLATELET VOLUME AS POTENTIAL PREDICTOR OF INTRADIALYTIC HYPERTENSION

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ABSTRAK

Kidney disease irregularities include platelets. Platelet disorders can harm renal and systemic blood flow. This study investigates whether platelet indices (mean platelet volume, platelet-lymphocyte ratio, and platelet count) might predict blood pressure changes before and after hemodialysis. This cross-sectional study included 98 Muhammadiyah University Malang General Hospital hemodialysis patients. Participants had to be 18 years or older, have been on hemodialysis for at least 1 month, and have given informed consent. IDHT incidence was the endpoint and MPV, PLR, and platelet count were predictors. Significant differences in systolic and diastolic blood pressure were observed between patients undergoing hemodialysis before and after hemodialysis ($p < 0.001$). Using the difference in systolic blood pressure before and after hemodialysis, a receiver operating characteristic (ROC) curve was created to evaluate the platelet count, MPV, and PLR markers' accuracy in predicting blood pressure increases during hemodialysis. According to the receiver operating characteristic (ROC) curve, MPV was highest above the diagonal line compared to PLR and platelet count with a 9.15 cut-off value. This suggests that MPV is the greatest prognostic metric.

Keywords: Blood pressure; Hemodialysis; Mean platelet volume (MPV); Platelet to lymphocyte ratio (PLR)

АБСТРАКТ

Нарушения при заболеваниях почек включают тромбоциты. Тромбоцитарные нарушения могут нарушить почечный и системный кровоток. В данном исследовании изучалось, могут ли показатели тромбоцитов (средний объем тромбоцитов, соотношение тромбоцитов и лимфоцитов и количество тромбоцитов) предсказывать изменения артериального давления до и после гемодиализа. В это перекрестное исследование были включены 98 пациентов, находящихся на гемодиализе в общей больнице Университета Мухаммадия Маланг. Участники должны были быть старше 18 лет, находиться на гемодиализе не менее 1 месяца и дать информированное согласие. Конечной точкой была заболеваемость ИДГТ, а предикторами - MPV, PLR и количество тромбоцитов. Значительные различия в систолическом и диастолическом артериальном давлении наблюдались между пациентами, находящимися на гемодиализе, до и после гемодиализа ($p < 0,001$). На основе разницы в систолическом артериальном давлении до и после гемодиализа была построена кривая приемных операционных характеристик (ROC) для оценки точности маркеров количества тромбоцитов, MPV и PLR в прогнозировании повышения артериального давления во время гемодиализа. Согласно кривой операционной характеристики приемника (ROC), MPV находился выше диагональной линии по сравнению с PLR и количеством тромбоцитов при значении отсечения 9,15. Это позволяет предположить, что MPV является наиболее прогностически значимым показателем.

Ключевые слова: Артериальное давление; гемодиализ; средний объем тромбоцитов (MPV); соотношение тромбоцитов и лимфоцитов (PLR)

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INTRODUCTION

Data from the 2013 to 2018 RISKESDAS reports show an increase in the prevalence of hypertension by 5.9% in Indonesia.[1] As a silent killer, uncontrolled hypertension can lead to various complications, even in patients undergoing hemodialysis. Recent studies have shown that patients with chronic kidney disease may experience increased blood pressure during and after hemodialysis. An increase in blood pressure during or immediately after hemodialysis, known as intradialytic hypertension, can lead to fatal consequences such as ischemic heart disease, heart failure, and even death.[1,2] The incidence of intradialytic hypertension is around 15–18% and can increase mortality by 20%.[1] To date, there are no recommendations or standard operating procedures (SOP) for early screening or management of intradialytic hypertension in patients undergoing hemodialysis.

Platelets are one of the components of blood cells that play a crucial role in maintaining vascular integrity and hemostasis.[3] Platelets also contribute to the regulation of inflammatory processes and the body's immune response. Vascular damage induces platelet aggregation, which plays a role in thrombus formation and may trigger thrombosis.[4] One indicator of platelet activity is the mean platelet volume (MPV). The larger the platelet size, the greater the potential for thrombosis and metabolic activity.[5] Previous studies have shown that larger platelet size/volume is associated with denser and more reactive platelet granules. These granules contain procoagulants that increase atherogenic potential, as well as Vascular Endothelial Growth Factor (VEGF), which contributes to thrombus formation in blood vessels.[6,7] Clinical observations have noted that patients undergoing hemodialysis due to kidney disease experience platelet abnormalities.[4] Measuring platelet components can help predict changes in blood pressure, allowing for better anticipation of undesirable outcomes in patients.

One determinant influencing blood pressure fluctuations is platelet count.[8] By calculating platelet index parameters—such as mean platelet volume (MPV) and the platelet-to-lymphocyte ratio (PLR)—early warnings of blood pressure changes in hemodialysis patients can be signaled. Previous research has suggested that the platelet-lymphocyte ratio (PLR) may serve as a systemic inflammatory indicator observed in hypertension, cardiovascular diseases, and malignancies. Additionally, PLR has been linked to inflammation and mortality prediction in patients with non-dialysis chronic kidney disease (CKD).[9] It is hoped that through the measurement of MPV and PLR, these markers can be developed as early detection tools for rising blood pressure, potentially mitigating the risk of morbidity and mortality among hypertensive patients, particularly those undergoing hemodialysis.

Previous studies have found that the MPV-to-platelet count ratio can serve as a cardiovascular mortality indicator,[8] although the research was conducted on patients under 60 years of age receiving peritoneal dialysis, not hemodialysis. Another study that calculated the neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) found a relationship between PLR and the gold standard of systemic inflammatory markers, namely C-reactive protein (CRP), in patients with non-hemodialysis chronic kidney failure.[9] CRP measurement is a specialized test, and not all laboratories are equipped to perform it. A cohort study on the East Asian population found an association between platelet count and both systolic and diastolic blood pressure, although the mechanism remains unclear.[10] Platelet count is one component of the complete blood count in patients undergoing hemodialysis, but this data has not yet been fully utilized, particularly as a potential predictor of changes in blood pressure. MPV and PLR calculations have demonstrated utility in stratifying mortality due to cardiac events and as prognostic factors in malignancy,[3] but their role in blood pressure changes, particularly in hemodialysis patients, is not yet

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clear. The aim of this study is to determine the relationship between mean platelet volume (MPV) and platelet-to-lymphocyte ratio (PLR) with changes in blood pressure before and immediately after hemodialysis.

MATERIAL AND METHODS

The study design is an analytical observational study with a cross-sectional approach. In this study, 98 patients undergoing hemodialysis at the Universitas Muhammadiyah Malang General Hospital were included. The participants were aged 18 years and older, had been on hemodialysis for at least 1 month, and had signed informed consent. The variables observed/measured include mean platelet volume (MPV), platelet count, and lymphocyte count from complete blood count results, as well as blood pressure before and immediately after hemodialysis. The calculated results will be tabulated and analyzed. Blood pressure differences will be tested using the Wilcoxon Rank Test, as the data are not normally distributed. Statistical significance is determined with a p-value < 0.05. The relationship between MPV, PLR, and platelet count with intradialytic blood pressure will be analyzed using receiver operating characteristic (ROC) curves to identify the most potential marker in predicting intradialytic hypertension. The cut-off point will be determined using the Youden J-index. Data analysis will be performed using IBM SPSS software 22.0.

RESULT

The study involved 108 patients undergoing hemodialysis. However, only 98 patients met the inclusion criteria (2 patients passed away, and data from 8 patients were incomplete). The youngest patient undergoing hemodialysis was 19 years old, and the oldest was 84 years old, with a mean age of 53.32±12.94 years. The majority of the patients were male (57 individuals), and most had been on hemodialysis for 1–5 years (73 individuals). Hypertension was the most common primary condition, affecting 73.47% of the patients. Most patients undergoing hemodialysis experienced anemia, with hemoglobin levels below 10 mg/dL. The average white blood cell and platelet counts were within normal ranges (4,000–11,000/uL; 185,000–450,000/uL). The mean platelet volume (MPV) was 9.17±0.99 fL, and the platelet-to-lymphocyte ratio (PLR) was 246.75±140.27.

Table 1. Characteristic Patients Undergoing Hemodialysis

Characteristics (n=98)	Value
Age (y.o.) (*mean±SD; range*)	53.32±12.94 (19-84)
Sex (n,%)	
- Male	57 (58.16)
- Female	41 (41.84)
Duration of Hemodialisis (years)(n,%)	
- < 1 years	15 (15.31)
- 1-5 years	73 (74.49)
- >5 years	10 (10.20)
Primary Disease (n,%)	
- Diabetes Mellitus (DM)	5 (5.1)
- Hypertension (HT)	72 (73.47)
- DM + HT	15 (15.31)
- Others	3 (3.06)
- None	3 (3.06)
Hemoglobin (g/dl) (rerata±SD)	8.39±1.39
Leucocyte Count (x 10^3/µL) (mean±SD)	6660.55±2447.04
Trombocyte Count (x 10^3/µL) (mean±SD)	259.03±84.73
Mean Platelet Volume (fL) (mean±SD)	9.17±0.99
Platelet Lymphocyte Ratio	246.75±140.27

There was a significant difference in the blood pressure of patients undergoing hemodialysis before compared to immediately after hemodialysis, for both systolic and diastolic blood pressure (p<0.001), as shown in Table 2.

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In light of the fact that the data did not follow a normal distribution, the Wilcoxon Rank Test was utilised in the analysis procedures. The systolic blood pressure was measured to be 127.87±11.01 mmHg before to the initiation of haemodialysis, whereas the diastolic blood pressure was measured to be 79.74±5.76 mmHg on average. Following haemodialysis, the average systolic blood pressure rose to 144.18±13.11 mmHg, while the average diastolic blood pressure rose to 86.53±6.47 mmHg. Both of these blood pressure measurements improved.

Table 2. Difference in Blood Pressure Before and After

	Before Hemodialysis (*mean±SD*)	Post-Hemodialysis (*mean±SD*)	*p-value*
Systolic Blood Pressure (mmHg)	127.87±11.01	144.18±13.11	<0.001*
Diastolic Blood Pressure (mmHg)	79.7449±5.76	86.53±6.47	<0.001*

Note: *Wilcoxon Rank Test, statistically significant if p<0.05

A receiver operating characteristic (ROC) curve was developed based on the difference in systolic blood pressure before and immediately after haemodialysis (Figure 1) in order to evaluate the sensitivity and specificity of the accuracy of the models for platelet count, MPV, and PLR in predicting the increase in blood pressure that occurs during IDHT. This was done in order to determine the accuracy of the models.

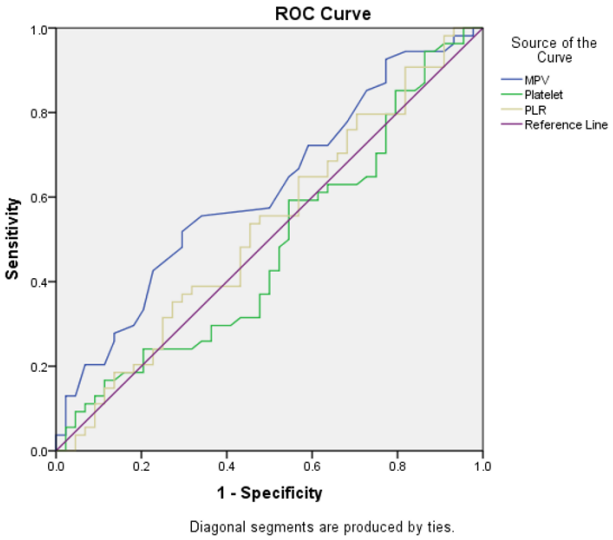

Figure 1: ROC Analysis of the Relationship Between Platelet Count, MPV, and PLR with Intradialytic Blood Pressure

Figure 1 illustrates the receiver operating characteristic (ROC) curves for platelet count, mean platelet volume (MPV), and platelet-to-lymphocyte ratio (PLR) in relation to changes in intradialytic blood pressure. Each curve indicates the model's ability to predict hypertension during hemodialysis. The area under the curve (AUC) values for each marker will provide insight into their diagnostic accuracy. From the generated ROC curve, it was observed that MPV (blue line) is positioned highest above the diagonal line (purple) compared to PLR and platelet count (MPV AUC = 0.615 vs PLR AUC = 0.529 vs Platelet AUC = 0.479), with a cutoff value for MPV according to the Youden J-index of 9.15. This indicates that MPV is the best predictive model when compared to the other models.

DISCUSSION

The study found that blood pressure before patients underwent hemodialysis showed a significant difference compared to blood pressure immediately after hemodialysis. Intradialytic hypertension almost always occurs in patients undergoing hemodialysis. The criteria for intradialytic hypertension include an increase in systolic blood pressure of more than 10 mmHg during hemodialysis or

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an increase in mean arterial pressure of more than 15 mmHg during or immediately after hemodialysis. This condition is associated with poor prognostics and an increased risk of mortality,[1,11]

The pathophysiology of hypertension in patients undergoing hemodialysis is multifactorial and differs from other populations. Several factors contributing to intradialytic hypertension include fluid overload, arterial stiffness, increased sympathetic nervous system activity, activation of the renin-angiotensin system, endothelial dysfunction, and the use of erythropoietin-stimulating agents.[12] Additionally, conventional hypertension risk factors such as older age, obesity, family history, and lack of physical activity also play a role in increasing blood pressure.

Mean Platelet Volume (MPV) or average platelet volume is considered one of the indicators of platelet function and activity. Larger platelets reflect higher platelet activity. Increased platelet activity leads to a greater concentration of prothrombotic cytokines and adhesion receptors. Platelets quickly move to the site of vascular endothelial injury, where they interact with collagen in the vessel wall and aggregate on top of the damaged endothelial cells. They are the first cells to gather at the site of injury, changing shape, forming pseudopodia, releasing cytoplasmic granular contents, and aggregating through the activation of inflammatory cytokines such as Interleukin (IL)-1, IL-6, and Tumor Necrosis Factor (TNF)-α.[13] This process results in hemostasis and thrombosis. Therefore, platelets are a crucial component of blood cells that play an important role in the pathophysiology of hemostasis and thrombosis. This is closely related to atherosclerotic cardiovascular diseases and other ischemic conditions.[8]

This study found that MPV serves as a better biomarker in predicting the increase in blood pressure for patients undergoing hemodialysis compared to the Platelet Lymphocyte Ratio (PLR) or platelet count. Although other studies have indicated that PLR can be used as an inflammatory marker in patients with Chronic Kidney Disease undergoing hemodialysis with malnutrition,[14] several other studies also emphasize the need for MPV measurements alongside platelet counts due to the non-linear inverse relationship between the two.[13] Increased MPV can be observed in chronic kidney disease, cardiovascular diseases, stroke, various types of cancer, diabetes, intestinal diseases, rheumatic conditions, and respiratory diseases. Conversely, decreased MPV has been noted in patients with exacerbated tuberculosis, lupus, and ulcerative colitis.[13]

Studies on MPV linked to increased blood pressure during hemodialysis (intradialytic hypertension) can provide important insights into the course and prognosis of inflammatory conditions. Determining the cutoff value for MPV that indicates the intensity of the inflammatory process, the presence of disease, the risk of disease progression, and the risk of thrombotic complications that can increase mortality risk is essential, as highlighted in this study.

The study also revealed significant differences in blood pressure before and after hemodialysis, suggesting that intradialytic hypertension is a common occurrence that can lead to severe complications and increased mortality risk. Additionally, the multifactorial nature of hypertension in this population involves factors such as fluid overload, arterial stiffness, and endothelial dysfunction, alongside conventional risk factors like age and obesity.

While the results indicate that MPV can serve as an effective clinical tool for monitoring and managing blood pressure in hemodialysis patients, further research is necessary to establish standardized MPV cutoff values and enhance its application in clinical practice. Overall, better assessment and management of intradialytic hypertension could significantly improve patient outcomes and quality of life.

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CONCLUSION

MPV emerged as a superior biomarker in predicting the occurrence of intradialytic hypertension in patients undergoing hemodialysis. However, evaluating MPV for potential clinical use requires further research. Better assessment and management of hypertension in patients undergoing hemodialysis can help extend and improve quality of life.

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DECLARATIONS

Author contribution. Idea/concept and research design: DS and AR. Data collection/processing: WD and AQ. Extraction/analysis/interpretation: DS, WD, AQ. Literatur review: DS, WD, AQ. Writing the article: DS. Critical review: DS, AR, WD, AQ. Control/supervision: AR. All authors have read and approved the final manuscript.

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