How to Cite:
Elwasif, S. M., Megahed, M. O., Elmoghazy, G., & Derbalah, S. A. (2022). Unravelling the role of MPV/platelets count on vascular access function among haemodialysis Egyptian patients: A retrospective single centre study. *International Journal of Health Sciences*, *6*(S3), 8060–8070. https://doi.org/10.53730/ijhs.v6nS3.7775

Unravelling the role of MPV/platelets count on vascular access function among haemodialysis Egyptian patients: A retrospective single centre study

Salwa Mahmoud Elwasif
Fellow of Internal Medicine and Nephrology, Urology and Nephrology Centre, Mansoura University, Egypt
ORCID: 0000-0001-5239-5567
*Corresponding author email: drsalwa22000@yahoo.com

Mohamed Osama Megahed
Assistant Lecturer of Internal Medicine, Damietta University, Egypt
ORCID: 0000-0003-2399-5752

Ghalia Elmoghazy
Fellow of Nursing, Quality Manager, Urology and Nephrology Centre, Mansoura University, Egypt
ORCID: 0000-0002-5813-0911

Safaa Awad Derbalah
Fellow of Medical Analysis, Clinical Pathology Unit, Urology and Nephrology Centre, Mansoura University, Egypt
ORCID: 0000-0003-4021-8234

***Abstract*---**Background and Aims: End-stage kidney disease (ESKD) is a global health problem. It necessitates renal replacement therapy via renal transplantation, peritoneal dialysis, or hemodialysis. Vascular access is mandatory for every patient maintained on hemodialysis. It is a prerequisite for adequate hemodialysis (HD). Platelets play the most important role in securing vascular access function. Patients and Methods: A retrospective cohort study was conducted on 87 patients who underwent intermittent HD via arteriovenous fistula (AVF). Patients were divided into two groups. Group1 (Study group): patients with recent thrombosed AVF within a week of laboratory investigation. Group2 (Control group): patients with well-functioning AVF Evaluation of patients: Results: The mean platelet volume (MPV), Plateletcrit (PCT), and platelet diameter width (PDW) were 10.43, 0.222, and 13.56 in the study group respectively while in the control

group they were 10.11067, 0.201944 and 12.9. MPV/PL count was significant between the two groups. Conclusion: The study found that the larger the platelet indices, the more vascular access malfunctions. The MPV/PL ratio can be used to examine the function of vascular access and estimate its lifespan that continuous monitoring of that ratio might be effective in detecting the risk of AVF in patients receiving regular hemodialysis.

***Keywords*---** AVF malfunction, hemodialysis, platelet indices.

Introduction

Hemodialysis (HD) is a type of renal replacement treatment for those who have kidney failure [1]. Every patient who requires HD must have vascular access (VA) to provide an effective blood flow rate throughout the HD session [2]. The most frequent kind of VA is an arteriovenous fistula (AVF) [3]. The procedure involves anastomosing the limb artery with its corresponding vein. For complete maturation of AVF and arterialization of veins to tolerate repeated cannulation with HD needles, it takes at least three weeks [4]. Platelets are crucial in the development of a typical atheroma, which can lead to peripheral arterial disease, coronary artery disease, and infarction. Even though circulating platelets vary in size and reactivity, it is widely assumed that larger platelets are metabolically and enzymatically more active and have a higher thrombotic potential than smaller platelets [5]. Using either the electrical impedance or optical fluorescence approach, automated blood analyzers calculate the mean platelet volume (MPV) [6].

It represents the platelet size distribution in a blood sample. As a result, MPV has received a great deal of interest as a promising measure of platelet function and activation. In patients with non-ST elevation acute coronary syndrome raised MPV has been linked to a greater risk of restenosis following coronary angioplasty and a higher rate of significant adverse cardiovascular events, according to many studies [7]. Patients with end-stage kidney disease (ESKD) are also susceptible to bleeding and thrombosis [8]. They have thrombasthenia and take anticoagulants throughout HD sessions, but they also have dehydration after dialysis, atherosclerosis, and extended recumbency, making it difficult to forecast what our patients require. Because of uremic thrombasthenia, the peripheral platelet count cannot predict platelet function [9]. As a result, in our study, we attempted to resolve this conundrum and ascertain a hint to anticipate or maybe cure AVF dysfunction in HD patients.

Patients and Methods

Patients' ethics declaration

This study was carried out in accordance with the Declaration of Helsinki and was approved by the Institutional Review Board (IRB) of the Urology and Nephrology Center, Mansoura University (Ref. 2021-04- 01-SM). The IRB waived the requirement for written permission because the study was retrospective and

the participants were de-identified. This study was performed on a total of 101 patients who received regular hemodialysis and met the inclusion criteria between May 2021 and March 2022. Patients had to be at least 18 years old, have been on HD for at least six months, and be reliant on AVF as permanent vascular access. Patients with a medical condition that might induce thrombophilia (antiphospholipid syndrome, polycythemia, etc.), an arteriovenous synthetic graft, a venous tunneled catheter, a history of congestive heart failure, or a previous vascular access surgical intervention were all excluded. A central venous tunneled catheter was used in 5 patients, while an arteriovenous synthetic graft was used in 9 others. As a consequence, the patients in the research were separated into two groups (n=87): group 1 included 21 patients with AVF malfunction, and group 2 had 66 patients with AVF that worked properly.

Research Methods

Patients were subjected to the following: full history taking, complete clinical examination including measurement of arterial blood pressure (Intradialytic hypotension is demarcated as the asymptomatic reduction in systolic blood pressure of 30 mmHg or a fall in mean blood pressure of 10 mmHg during dialysis) [10], and BMI. Furthermore, an auto-analyzer (Sysmex XN-9100TM Automated Hematology System) was used to analyze laboratory parameters such as MPV level, PL count, and hemoglobin (Hgb) level from blood samples. Routine serum biochemical tests were evaluated by an auto-analyzer (Beckman Coulter AU5800; Beckman Coulter Inc., Brea, California, USA). Kt/V was designed in line with the procedure of Gotch [11]. URR (urea reduction ratio) was premeditated by the formula: 1− (post-BUN/pre-BUN) [12]. The AVF's flow rate (FR) and velocity were measured using Doppler ultrasonography.

Statistical analysis

GraphPad Prism version 8.2 was used to collect and analyze the data. The relationship between qualitative variables was measured using the x2-Test. Fisher exact test was applied for 2*2 qualitative variables. When the data were not normally distributed, the Mann–Whitney test (U) was employed to compare the mean and SD of two sets of quantitative normally distributed data. The receiver operating characteristic curve (ROC) was used to find the cutoff value that had the best sensitivity and specificity. The following metrics were calculated: sensitivity, specificity, and diagnostic accuracy.

Results

Baseline characteristics of the studied groups

The baseline characteristics of the study patients are publicized in Table 1. The mean age was 50.38 ±5.96 years and 42.63 ±5.66 for the studied groups respectively with a predominance significance of males between the two groups. There was no statistically significant difference between functioning and dysfunctioning groups regarding their age, duration of hemodialysis, AVF in dominance, Kt/V, and BMI (P=0.051, 0.93, 0.144, and 0.205 respectively). There was a statistically significant difference between functioning and dysfunctioning

groups regarding intradialytic hypotension, as 80.95 % of the dysfunctioning group had intradialytic hypotension compared with 46.96 % of the functioning group (P=0.043); however, there was no statistically significant difference between functioning and dysfunctioning groups regarding Hgb, Hct, calcium, and phosphorus (P= 0.219, 0.799, 0.374, and 0.114, respectively). There was a statistically significant difference between the study groups regarding PL count, showing a higher PL count in the functioning group (215.75/10^3) than in the dysfunctioning group (155.2/10^3).

Table 1
Bassline characteristics of laboratory and clinical data of both studied groups

Parameters	Study group (AVF dysfunction) No= 21	Control group (Functioning AVF) No=66	P-value
Age (Mean ± SD)	50.38 ±5.96	42.63 ±5.66	0.051
Sex (Male/Female)	12/9	43/23	>0.001
Duration of hemodialysis in months (Mean± SD)	108 ±28.6	103.4±30.5	0.93
Intradialytic hypotension - Yes - No	 17 (80.95%) 4 (19.04%)	 31 (46.96%) 35 (53.03%)	0.043
AVF in dominant versus non-dominant hand	8/13	18/48	0.513
Kt /V (mean ± SD)	1.22± 0.233	1.32± 0.259	0.144
Hgb gm/dl (mean ± SD)	10.67 ± 2.7	11.64 ± 3.01	0.219
Hct (Mean±SD)	32.70 ± 3.62	32.33 ± 5.61	0.799
Plt count/10^3 (Mean±SD)	155.2± 75.13	215.75 ± 72.23	0.023
Ischemic heart disease (present/absent)	13/8	30/36	>0.001
Serum calcium (Mean±SD)	9.03±0.93	9.25±0.92	0.374
Serum phosphorus (Mean±SD)	5.011±1.53	5.695± 1.62	0.114
Serum cholesterol (Mean± SD)	134.9 ±2.09	136.3±0.99	0.041
Urea reduction ratio (Mean ± SD)	59.51±2.36	68.9±5.62	0.012
Body mass index: - <18.5 - 18.6-24.9 - 25-29.9 - >30	 1 9 7 4	 7 33 19 7	0.205

SD, standard deviation. Hgb, hemoglobin. Plt, platelet count, Hct, hematocrit.

Comparison of Platelets indices in both studied groups

The mean platelet volume (MPV) of the dysfunctioning group was lower than the functioning group (8.05±1.06) (P=0.04) when the MPV was compared in both groups. Furthermore, there were significant variations in MPV/PL between the two groups (P=0.01). PCT and PDW, on the other hand, were not statistically significant as revealed in Table 2.

Table 2
Comparison of Platelets indices in both studied groups

Parameters	Study group (AVF dysfunction) No= 21	Control group (functioning AVF) No=66	P-value
MPV (Mean±SD)	8.05±1.06	10.09 ± 0.94	0.04
MPV/PL count (Mean±SD)	61.20 ± 3.12	55.3 ± 4.98	0.01
PCT (Mean±SD)	0.211±0.068	0.201 ±0.07	0.30
PDW	13.3 ±2.96	12.98 ± 2.37	0.28

MPV, mean platelet volume. MPV/PL count ratio, mean platelet volume/platelet count ratio. PCT, Plateletcret. PDW, platelet diameter width. AVF, arteriovenous fistula. SD, standard deviation

Valuation of arteriovenous fistula in the study population

In terms of fistulas with difficult cannulation, there was a statistically significant difference between the study groups, with 57.14 % of group 1 having a functioning fistula with difficult cannulation compared to 10.60 % of group 2. In terms of arm elevation test, there was a statistically significant difference between the study groups, with % of group 2 having a positive result compared to 9.52 % of group 1. There was a statistically significant difference in the history of ischemia between the two groups tested, with 80.96 % of group 1 having a history of ischemia compared to 0.0 % of group 2. Table 3 shows that there was no statistically significant difference between the study groups when it came to thrombosis history and AVF age.

Table 3
Clinical assessment of the arteriovenous fistula in the studied groups

AVF Appearances	Study group (AVF dysfunction) N= 21	Control group (functioning AVF) N=66	P-value
History of thrombosis (n, %) - No - One - Two	 18 (85.7%) 2 (9.52%) 1 (4.76%)	 53 (80.30%) 7 (10.60%) 6 (9.09%)	0.056
AVF age (months) (Mean±SD)	18.5±5.89	21.32±6.87	0.621
Fistula with difficult cannulation (n, %) - No - Yes	 9 (42.85%) 12 (57.14%)	 59 (89.39%) 7 (10.60%)	> 0.001
Arm elevation test (n, %) - -ve - +ve	 19 (90.47%) 2 (9.52%)	 0 (0.0) 66 (100%)	>0.001
Ischemia (n, %) - Yes - No	 17 (80.96%) 4 (19.04%)	 0 (0.0) 66 (100%)	>0.001

Doppler appearances in all participants

By studying Doppler appearances of the AVF, our findings indicated statistically significant differences between the study groups in terms of velocity and flow rate, but no statistically significant differences in terms of arterial and venous diameter, as shown in Table 4.

Table 4
Doppler appearances of the AVF among the studied groups

Doppler data	Study group (AVF dysfunction) N= 21	Control group (functioning AVF) N=66	Mann-Whitney *U* test	P-value
Arterial diameter (mm) (Mean±SD)	4.04±1.13	4.6±1.05	1.42	0.058
Venous diameter (mm) (Mean±SD)	6.02±2.7	7.02±3.5	0.745	0.158
Velocity (Mean±SD)	16.7±37.6	97.1±43.9	4.91	>0.001
Flow rate (ml/min) (Mean±SD)	209.6±44.24	993.7±188.12	4.42	>0.001

Receiving operating characteristics (ROC) for MPV/PL count ratio prediction

The cutoff value of the MPV/PL ratio, which can diagnose AVF function in Egyptian hemodialysis patients, was determined using the receiver operating characteristic (ROC). The best cutoff point was 58.7, as shown in Figure 1, with an area under the curve (AUC) of 0.879. As indicated in Table 5, the sensitivity was 92.5 percent, the specificity was 81 %, the positive predictive value was 0.830 (95 % CI: 0.921 to 0.920), and the negative predictive value was 0.305 (95 % CI: 0.202 to 0.376).

Table 5
Receiving operating characteristics (ROC) for MPV/PL count prediction of AVF

Area under the ROC curve (AUC)	0.879
Standard Error	0.28
95% Confidence interval	(0.870 - 0.947)
Significance level P (Area=0.5)	0.004
Youden index	0.53
Sensitivity	92.5
Specificity	81.0
Optimal cutoff point	58.7

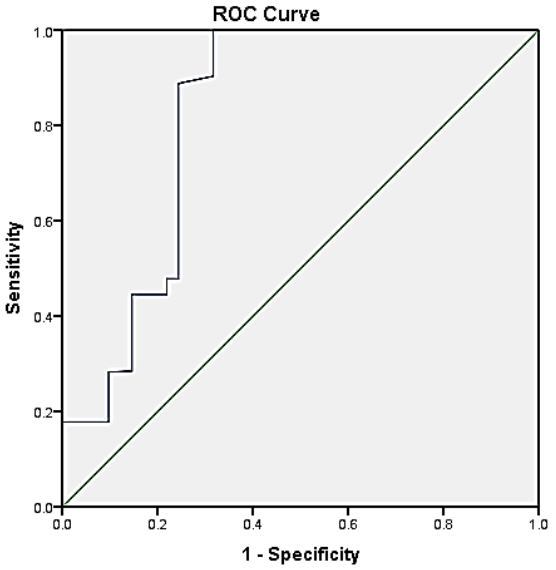

Figure 1. ROC of MPV/PL count for predicting AVF function in Egyptian hemodialytic patients

Discussion

The hemodialysis (HD) patient requires well-functioning vascular access; nonetheless, HD vascular access failure remains one of the most common causes of morbidity in the HD population [13]. The gradual development of neointimal hyperplastic stenosis is a common cause of HD vascular access impairment [14]. These lesions increase intra-access resistance, which reduces blood flow and leads to thrombosis, which is the most common cause of HD vascular access failure [15]. Our research is a retrospective cohort study that examines the many parameters that influence the function of arteriovenous fistulas in hemodialysis patients. Our data revealed that there was no statistically significant difference between the functional and dysfunctioning groups in terms of age, Kt/V, and BMI. Contrary to popular opinion, older age, diabetes, male sex, obesity, cardiovascular illness, and smoking have all been linked to VAF in HD patients [16], [17]. A modest sample size might justify this. Intradialytic hypotension was shown to differ significantly between the two groups in our investigation.

In this study, there were no significant differences between both groups as regard duration of hemodialysis and the presence of AVF in the non-dominant hand. These findings were supported by Turkish research that found that, despite no difference in infection rates, having AVF in the non-dominant arm improves the quality of life of patients [18]. Our data showed that an increase in MPV/PL count ratio was significantly associated with VAF. This comes in line with other studies [19]. In our study, there was high MPV in a group of AVF dysfunction that was similar to that reported in a study of 163 chronic hemodialysis patients by Abdelmagid et al [20]. The difference in URR between the two groups was exceptionally significant in our study. Other research [21], [22] has found the same finding. According to Doppler on AVF, there was a substantial difference

between the two groups in terms of flow rate and velocity, with group 2 having a greater velocity. This finding agrees with that of Ahmed et al [19], who revealed a substantial variation in Doppler parameters (flow rate, velocity, and resistive index) in HD patients depending on AVF function, finding that these values were high in patients with functioning AVF.

Although several monitoring and surveillance approaches exist to detect arteriovenous vascular access dysfunction, the choice is influenced by several factors, the most important of which are vascular access type, technology, operator effect, and cost [23]. As a result, developing simple, cost-effective, and universal approaches to test for the risk of VAF in hemodialysis patients is critical. Platelet reactivity is an important factor to consider since platelets play a crucial role in vascular disease [24]. Platelet dysfunction has been found in uremic patients due to reduced platelet aggregation and poor platelet adhesion [25]. It might be caused by platelet granule disruption, altered Ca+ metabolism, decreased GP IIb/IIIa function, and reduced vWF and fibrinogen binding in uremic patients [26].

On the contrary, elevated levels of phosphatidylserine, P-selectin, and fibrinogen receptor PAC-1 in platelets have been linked to an increased risk of thrombosis in uremic patients [27]. Although nothing is understood about why one uremic patient has bleeding while another experiences severe thrombus development, a generic approach for measuring platelet reactivity is required. Several studies have found a link between MPV and vascular disease [28], [29]. MPV was found to be an independent predictor of acetylcholine-induced coronary vasospasm in research by Leader et al. [30]. Berger et al. found that an increase in MPV was independently linked with peripheral artery disease, as defined by an ankle-brachial index of 0.90 in either leg [31].

The platelet count and MPV are often negatively associated [32]. As a result, a higher MPV/platelet count ratio indicates a higher MPV and a lower platelet count. Furthermore, a drop in platelet count might suggest coagulation system activity. Multiple investigations have linked a low platelet count to elevated glycoprotein VI and inflammatory markers, suggesting that platelet activation is enhanced in cardiovascular disease [33], [34]. Williams et al. [56] found that heparin-induced thrombocytopenia may have a role in recurrent ischemia episodes in individuals with the acute coronary syndrome [35]. As a result, the MPV/platelet count ratio may be more useful in predicting platelet reactivity than MPV alone. Han et al. found that the MPV/platelet count ratio might be a more effective predictor of deep vein thrombosis than MPV alone [36].

Conclusion

Our study found that in hemodialysis patients, a rise in the MPV/platelet count ratio over time was independently linked with VAF. Although more research is needed to fully understand the function of the MPV/platelet count ratio as a risk factor for VAF, the findings imply that continuous monitoring of the ratio might be effective in detecting the risk of VAF in patients receiving regular hemodialysis.

Conflict of interest

All authors declare that there is no conflict of interest

Author contribution

Conceptualization: SME, MOM. Data curation: SME, GE. Formal analysis: SAD, MOM. Investigation: SME Methodology: SAD, SME. Supervision: SME. Visualization: SME, MOM, SAD. Writing – review & editing: All authors

Fund

Neither fund nor grant was taken

References

1. Murea M, Moossavi S, Fletcher AJ, Jones DN, Sheikh HI, Russell G, Kalantar-Zadeh K. Renal replacement treatment initiation with twice-weekly versus thrice-weekly haemodialysis in patients with incident dialysis-dependent kidney disease: rationale and design of the TWOPLUS pilot clinical trial. BMJ Open. 2021;11(5):e047596.
2. Kalantari K. The choice of vascular access for therapeutic apheresis. J Clin Apher. 2012;27(3):153–9.
3. Leermakers J, Bode AS, Vaidya A, Van Der Sande FM, Evers S, Tordoir JHM. Cost-effectiveness of vascular access for haemodialysis: arteriovenous fistulas versus arteriovenous grafts. Eur J Vasc Endovasc Surg. 2013;45(1):84–92.
4. Dinwiddie LC, Ball L, Brouwer D, Doss-McQuitty S, Holland J. What nephrologists need to know about vascular access cannulation. In: Seminars in Dialysis. Wiley Online Library; 2013. p. 315–22.
5. Schrottmaier WC, Mussbacher M, Salzmann M, Assinger A. Platelet-leukocyte interplay during vascular disease. Atherosclerosis. 2020;307:109–20.
6. Zsóri KS, Mahalek JM, Mokarrami MA, Csiki Z, Shemirani AH. Preanalytical factors affecting the mean platelet volume: a review. Glob J Hematol Blood Transfus. 2016;3(1):19–22.
7. Ju HY, Kim JK, Hur SM, Woo SA, Park KA, Park MY, Choi SJ, Hwang SD. Could mean platelet volume be a promising biomarker of progression of chronic kidney disease? Platelets. 2015;26(2):143–7.
8. Aziz AFA, Saad ATA, Bazeed MM, Allam MAR, Bakeer MS. A comparative study of platelet parameters in chronic kidney disease, end stage renal disease patients undergoing hemodialysis and healthy individuals. Egypt J Hosp Med. 2018;71(6):3429–33.
9. Himmelfarb J, Chuang P, Schulman G, Adequacy H, Prescriptions A, Hemodialysis C. Brenner & Rector's The Kidney. 2008;
10. Parsegian K, Trivedi R, Ioannidou E. Renal Diseases. Burket's Oral Med. 2021;579–626.

11. Diaz-Buxo JA, Loredo JP. Standard Kt/V: comparison of calculation methods. Artif Organs. 2006;30(3):178–85.
12. Chertow GM, Owen WF, Lazarus JM, Lew NL, Lowrie EG. Exploring the reverse J-shaped curve between urea reduction ratio and mortality. Kidney Int. 1999;56(5):1872–8.
13. Ethier J, Mendelssohn DC, Elder SJ, Hasegawa T, Akizawa T, Akiba T, Canaud BJ, Pisoni RL. Vascular access use and outcomes: an international perspective from the Dialysis Outcomes and Practice Patterns Study. Nephrol Dial Transplant. 2008;23(10):3219–26.
14. Lin C-C, Chang C-F, Lai M-Y, Chen T-W, Lee P-C, Yang W-C. Far-infrared therapy: a novel treatment to improve access blood flow and unassisted patency of arteriovenous fistula in hemodialysis patients. J Am Soc Nephrol. 2007;18(3):985–92.
15. Mima A. Hemodialysis vascular access dysfunction: molecular mechanisms and treatment. Ther Apher Dial. 2012;16(4):321–7.
16. Longenecker JC, Coresh J, Powe NR, Levey AS, Fink NE, Martin A, Klag MJ. Traditional cardiovascular disease risk factors in dialysis patients compared with the general population: the CHOICE Study. J Am Soc Nephrol. 2002;13(7):1918–27.
17. Kazancioğlu R. Risk factors for chronic kidney disease: an update. Kidney Int Suppl. 2013;3(4):368–71.
18. Erkut B, Ünlü Y, Ceviz M, Becit N, Ateş A, Çolak A, Koçak H. Primary arteriovenous fistulas in the forearm for hemodialysis: effect of miscellaneous factors in fistula patency. Ren Fail. 2006;28(4):275–81.
19. Ahmed HA, Emara MM, Kasem HE, Tahoon MAH. Effect of the mean platelet volume/platelet count ratio on arteriovenous fistula function in chronic hemodialysis patients. Menoufia Med J. 2021;34(1):129.
20. Abdelmagid EHE, Hassan BA, Ibrahim HE. Mean Platelet Volume/Platelet Count Ratio as Screening for Vascular Access Failure in Children on Regular Hemodialysis. Ann Rom Soc Cell Biol. 2021;25(6):6950–61.
21. Kalantar-Zadeh K, Kleiner M, Dunne E, Lee GH, Luft FC. A modified quantitative subjective global assessment of nutrition for dialysis patients. Nephrol Dial Transplant Off Publ Eur Dial Transpl Assoc Ren Assoc. 1999;14(7):1732–8.
22. Mehta RL, Mcdonald B, Gabbai FB, Pahl M, Pascual MTA, Farkas A, Kaplan RM, ICU CG for T of ARF in the. A randomized clinical trial of continuous versus intermittent dialysis for acute renal failure. Kidney Int. 2001;60(3):1154–63.
23. Kumbar L, Karim J, Besarab A. Surveillance and monitoring of dialysis access. Int J Nephrol. 2012;2012.
24. Ed Nignpense B, Chinkwo KA, Blanchard CL, Santhakumar AB. Polyphenols: modulators of platelet function and platelet microparticle generation? Int J Mol Sci. 2019;21(1):146.

25. Benson KK, Quimby JM, Shropshire SB, Summers SC, Dowers KL. Evaluation of platelet function in cats with and without kidney disease: a pilot study. J Feline Med Surg. 2021;23(8):715–21.
26. Lutz J. Platelets in advanced chronic kidney disease: two sides of the coin. In: Seminars in thrombosis and hemostasis. Thieme Medical Publishers; 2020. p. 342–56.
27. Roka-Moiia Y, Walk R, Palomares DE, Ammann KR, Dimasi A, Italiano JE, Sheriff J, Bluestein D, Slepian MJ. Platelet activation via shear stress exposure induces a differing pattern of biomarkers of activation versus biochemical agonists. Thromb Haemost. 2020;120(05):776–92.
28. Wada H, Dohi T, Miyauchi K, Shitara J, Endo H, Doi S, Tsuboi S, Ogita M, Iwata H, Kasai T. Mean platelet volume and long-term cardiovascular outcomes in patients with stable coronary artery disease. Atherosclerosis. 2018;277:108–12.
29. Mohammed HA, Amin ME, Mahmoud MG. Mean platelet volume as a biomarker of the risk and prognosis of coronary artery disease. Sohag Med J. 2019;23(2):38–41.
30. Leader A, Pereg D, Lishner M. Are platelet volume indices of clinical use? A multidisciplinary review. Ann Med. 2012;44(8):805–16.
31. Berger JS, Eraso LH, Xie D, Sha D, Mohler III ER. Mean platelet volume and prevalence of peripheral artery disease, the National Health and Nutrition Examination Survey, 1999–2004. Atherosclerosis. 2010;213(2):586–91.
32. Sloan A, Gona P, Johnson AD. Cardiovascular correlates of platelet count and volume in the Framingham Heart Study. Ann Epidemiol. 2015;25(7):492–8.
33. Azab B, Torbey E, Singh J, Akerman M, Khoueiry G, Mcginn Jr JT, Widmann WD, Lafferty J. Mean platelet volume/platelet count ratio as a predictor of long-term mortality after non-ST-elevation myocardial infarction. Platelets. 2011;22(8):557–66.
34. Han JS, Park TS, Cho SY, Joh JH, Ahn HJ. Increased mean platelet volume and mean platelet volume/platelet count ratio in Korean patients with deep vein thrombosis. Platelets. 2013;24(8):590–3.
35. Davoren A, Aster RH. Heparin-induced thrombocytopenia and thrombosis. Am J Hematol. 2006;81(1):36–44.
36. Shin DH, Rhee SY, Jeon HJ, Park J-Y, Kang S-W, Oh J. An increase in mean platelet volume/platelet count ratio is associated with vascular access failure in hemodialysis patients. PLoS One. 2017;12(1):e0170357.