



Original Article

The association between mean platelet volume and inflammation in geriatric patients with emergency hypertension

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ABSTRACT

Objectives: We aimed to investigate the role of inflammation parameters and platelet activation in geriatric patients with hypertension. Therefore, we compared the levels of those parameters in patients with hypertensive urgency and emergency. We also investigated the potential relationship between those parameters.

Methods: Ninety-six hypertensive (HT) patients (aged > 60) were included in the study in two groups: HT emergency (N = 48, group 1) and HT urgency (N = 48, group 2). Mean platelet volume (MPV), neutrophil-to-lymphocyte ratio (NLR) and high-sensitive C reactive protein (hs-CRP) were compared between those groups. Optimum cut-off levels of each parameter were determined by the use of Receiver operating characteristic (ROC) curve analysis. Pearson correlation test was used to examine the relationship between variables.

Results: The mean MPV and hs-CRP levels were significantly higher in patients with HT emergencies (both $P < 0.001$). Mean NLR was also significantly different between the two groups ($P = 0.011$). Pearson correlation analysis revealed a positive but weak correlation between the MPV and NLR ($r = 0.245$, $P = 0.016$), the hs-CRP level ($r = 0.394$, $P < 0.001$), and the WBC count ($r = 0.362$, $P < 0.001$).

Conclusion: Increased platelet activity and inflammation are associated with the end organ failure. Levels of MPV and other inflammatory parameters may be useful in the management of geriatric patients with HT.

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1. Introduction

In parallel with the increase in world population, life expectancy and the percentage of the seniors are increasing worldwide (1). Thus, the health problems caused by hypertension (HT) and other cardiovascular diseases are more frequent in elderly patients. High blood pressure (BP) in the elderly is potentially life-threatening and may trigger various complications. BP should be reduced within 1–2 h in patients with HT emergencies to prevent or restrict organ damage. Inflammation plays a significant pathophysiological role in HT (2,3). The number of giant hyperaggregable platelets is increased, and platelet activation is enhanced, increasing the mean

platelet volume (MPV), which plays a significant role in the progression of acute coronary and peripheral artery disease (4,5). Indeed, an increased MPV damages the coronary artery (CA) and can trigger myocardial infarction (MI) within hours (4). Patients with HT are often at prothrombotic or hypercoagulable state. Primary complications of HT are usually thrombotic, and this increase in MPV often triggers thrombotic complications. Increased platelet activation is associated with increased cardiovascular morbidity and mortality in hypertensive patients. Several studies have shown that the MPV is a marker for cardiovascular risks and a predictor of thrombotic complications in hypertensive patients (6).

Although both the MPV and inflammation were studied in the context of cardiovascular disease, including hypertensive crisis, little is known about their roles in geriatric patients with HT admitted to emergency departments (EDs) (5).

We aimed to investigate the role of inflammatory parameters, such as MPV, high-sensitive C-reactive protein (hs-CRP), and a neutrophil-to-lymphocyte ratio (NLR) in geriatric patients

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admitted to an ED in a hypertensive state. Therefore, we compared the level of MPV and those inflammatory parameters in patients with HT emergency and urgency.

2. Methods

2.1. Study setting

This study was conducted as a prospective observational study between January 2017–November 2017 in a single ED. The study protocol adhered to the dictates of the 1989 Declaration of Helsinki and approved by the Ethics Committee of Diyarbakir Gazi Yasargil Research and Training Hospital (Date: 17.07.2017, Approval number:73).

2.2. Study population

All geriatric patients (aged > 60 years) admitted to our ED with a hypertensive emergency or urgency during the study period were prospectively recruited (n = 96). Patients were grouped according to clinical severity: HT emergency (N = 48, group 1) and HT urgency (N = 48, group 2). HT emergency was defined as the elevation of BP with the evidence of target organ failure: acute coronary syndrome, acute heart failure, acute pulmonary edema, cerebrovascular event, aortic dissection, hypertensive encephalopathy, hypertensive retinopathy, and acute renal failure. Patients who admitted to ED with severely elevated BP without end-organ injury or failure were classified as HT urgency (7).

2.3. Exclusion criteria

Patients with pulmonary hypertension, chronic heart disease, any chronic respiratory disorder, rheumatological disease, uncontrolled diabetes mellitus, any other chronic inflammatory process, hepatic or renal failure were excluded. No patient was on anticoagulant or antiplatelet drug therapy (including aspirin) at the time of admission.

2.4. Clinical assessment

All patients with HT and its complications were evaluated. First, a physical examination was performed. Then blood was sampled for study tests (including the NLR) and biochemical assays (including a troponin assay). All vital signs, including BP, were measured and monitored during the stay. Written informed consent was obtained from the patient or legal guardians. Basic and advanced life support was provided at the time of ED presentation if necessary. Elevated BP was managed as appropriately with the use of antihypertensive drugs. Brain computed tomography and echocardiography were performed, if necessary. Patients with HT emergencies were admitted to neurology, nephrology or cardiology wards for further evaluation and management. Patients with HT urgencies were discharged after a brief period of BP and symptom monitorization in the ED.

2.5. Measurements and data collection

BPs was measured using the first and fifth phases of the Korotkoff sound, by a cuff sphygmomanometer. Body mass index (BMI) was calculated as the weight divided by the height squared (kg/m²). The body surface area (BSA, m²) of each patient and other clinical characteristics were also recorded. Blood samples were drawn from the antecubital vein as soon as patients were admitted to ED. All of the measurements were performed within 1 h of venipuncture to prevent in-vitro platelet activation. Blood

specimens were collected into ethylenediaminetetraacetic acid (EDTA) containing tubes and analyzed with the aid of a Cell-Dyn 4000 cell counter (Abbott; North Chicago, IL, USA) using commercial kits (Abbott, USA). The normal MPV was accepted as 6.8–10.8 fL. NLR was calculated from the levels of neutrophils and lymphocytes, manually. The levels of plasma triglycerides, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, creatinine, glucose, hemoglobin, and the creatine-kinase MB isoenzyme were measured using commercial kits. Hs-CRP levels were measured with the aid of an Aeroset autoanalyzer using a commercial spectrophotometric kit (Abbott, USA).

2.6. Statistical analysis

We estimated the sample size as 48 cases in each group, for an effect size of d = 0.5 and a type 1 error of 5%. The minimum post-hoc power of the study to discriminate the mean values between groups was calculated as 0.78. All statistical analyses were performed with SPSS v20.0 (IBM Inc., USA). Continuous variables with normal distributions were presented with means, standard deviations and 95% confidence intervals and compared using the Student's t-test. Categorical variables were summarized with counts and frequencies and compared with the chi-squared test. Receiver operating characteristic (ROC) curve analysis was used to determine the optimum cut-off level of MPV in patients with HT admitted to ED. Pearson correlation test was used to explore the

Table 1

Baseline demographic and clinical characteristics of the patients with hypertensive emergency and urgency

| Variable | HT emergency (n = 48, 50%) | HT urgency (n = 48, 50%) | P |
|-------------------------------------|-------------------------------|-----------------------------|-------|
| Age (years), mean (SD) | 67.8 (12.4) | 64.5 (10.7) | 0.469 |
| Male, n (%) | 28 (58.3) | 30 (62.5) | 0.835 |
| DM, n (%) | 10 (20.8) | 8 (16.7) | 0.273 |
| BMI (kg/m ²), mean (SD) | 26.9 (2.4) | 27.9 (2.2) | 0.098 |
| SBP (mmHg), mean (SD) | 174.1 (14.3) | 174.1 (14.7) | 0.160 |
| DBP (mmHg), mean (SD) | 109.0 (8.9) | 103.9 (9.7) | 0.009 |
| HR (bpm), mean (SD) | 108.4 (19.9) | 107.2 (17.6) | 0.476 |

p < 0.05 was accepted as statistically significant for student t-test (continuous data) and chi-squared test (categorical data). DM: diabetes mellitus, BMI: body mass index, SBP: systolic blood pressure, DBP: diastolic blood pressure, HR: Heart rate,

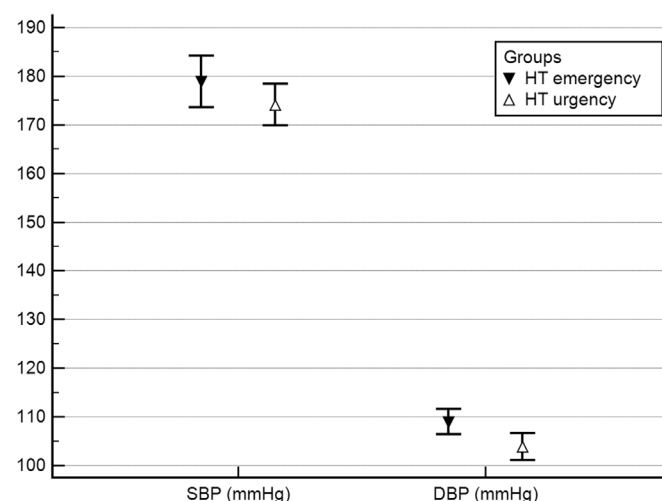


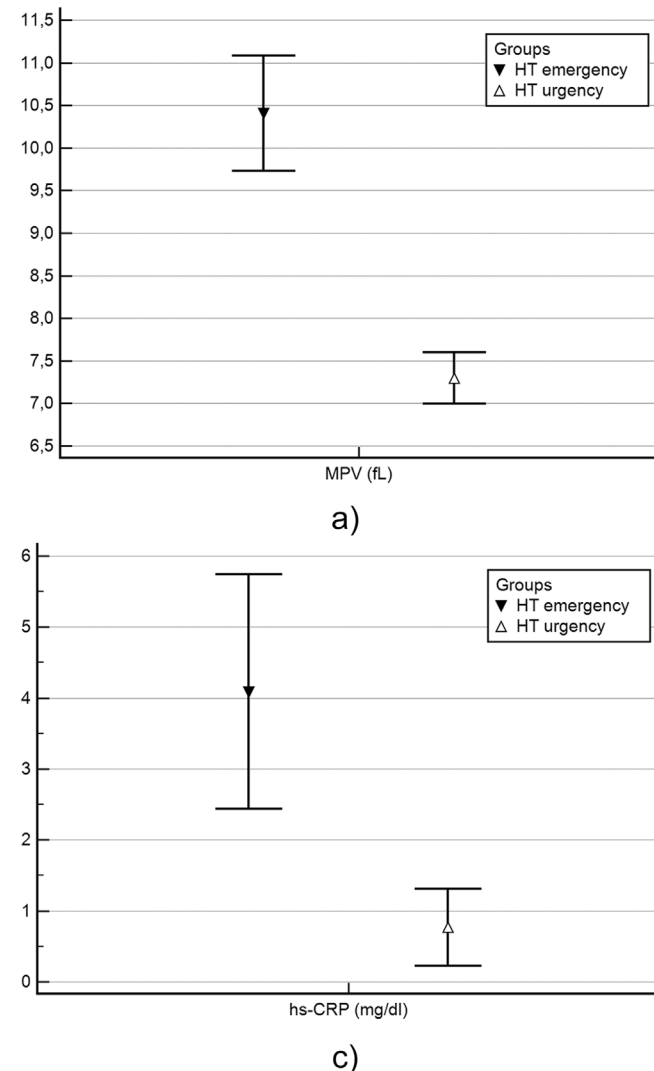
Fig. 1. Baseline characteristics of SBP and DBP in geriatric patients with HT emergency and urgency.

Table 2
Baseline laboratory characteristics of the patients with Emergency and Emerged HT

| Variables, mean (SD) | HT emergency (n = 48, 50%) | HT urgency (n = 48, 50%) | P |
|---------------------------|-------------------------------|-----------------------------|--------|
| HDL (mg/dl) | 38.6 (8.1) | 44.8 (11.7) | 0.003 |
| LDL (mg/dl) | 114.3 (31.3) | 127.0 (28.2) | 0.039 |
| TG (mg/dl) | 154.3 (87.4) | 155.2 (56.6) | 0.953 |
| Creatinine (mg/dl) | 0.9 (0.3) | 0.8 (0.2) | 0.822 |
| WBC (10 ³ /μl) | 11.98 (4.12) | 7.87 (2.13) | <0.001 |
| PLT (x10 ⁹ /L) | 268.6 (89.9) | 281.1 (63.8) | 0.434 |
| Hgb (g/dL) | 13.23 (1.89) | 13.45 (1.77) | 0.565 |
| CK-MB (ng/dL) | 2.37 (0.96) | 2.09 (0.91) | 0.149 |
| Troponin I (ng/dL) | 35.17 (29.29) | 17.81 (8.74) | <0.001 |
| APTT (sec) | 25.84 (6.08) | 27.91 (4.68) | 0.065 |
| Hs-CRP (mg/dl) | 4.09 (5.68) | 0.77 (1.86) | <0.001 |
| NLR | 4.12 (4.76) | 2.23 (1.54) | 0.016 |
| MPV (fL) | 10.41 (2.33) | 7.29 (1.04) | <0.001 |

p < 0.05 was accepted as statistically significant for student t-test. APTT: activated partial thromboplastin time, CK-MB: creatinine-kinase MB fraction, Hgb: hemoglobin, HDL: high-density lipoprotein, hs-CRP: high-sensitive C-reactive protein, LDL: low-density lipoprotein, MPV: mean platelet volume, NLR: neutrophil-to-lymphocyte ratio, PLT: platelets, TG: triglyceride, WBC: white blood cell.

relationships among variables. The overall type 1 error accepted in this study was 5%.



3. Results

There were 48 (50%) patients in HT emergency and urgency groups. Clinical and demographic parameters of the study population are shown in Table 1. No significant difference was observed according to those variables between study groups. The demographic characteristics of the two groups were similar.

The end-organ injury/failures of hypertensive emergencies were distributed as follows: 22 (45.8%) pulmonary edema, 11 (22.9%) acute MIs, 9 (18.8%) transient ischemic attacks, and 6 (12.5%) acute renal failure (ARF). Eight (16.7%) patients with HT emergency experienced a cardiac arrest within 24 h of ED admission, and 3 (6.3%) were lost within 30 days. At the time of blood sampling, no patient was on an antihypertensive drug. After the diagnosis was confirmed, all patients (N = 96) were treated with antihypertensive drugs. The mean SBP levels were similar in hypertensive emergency and urgency groups (Table 1, Fig. 1). In contrast, the mean DBP was slightly but significantly lower in HT urgency group (P = 0.009).

The comparison of MPV, NLR, hs-CRP levels is shown in Table 2 and Fig. 2. All three parameters were significantly higher (both statistical and clinical) in patients with HT emergencies (Table 2). NLR was also higher in HT emergency group despite a similar

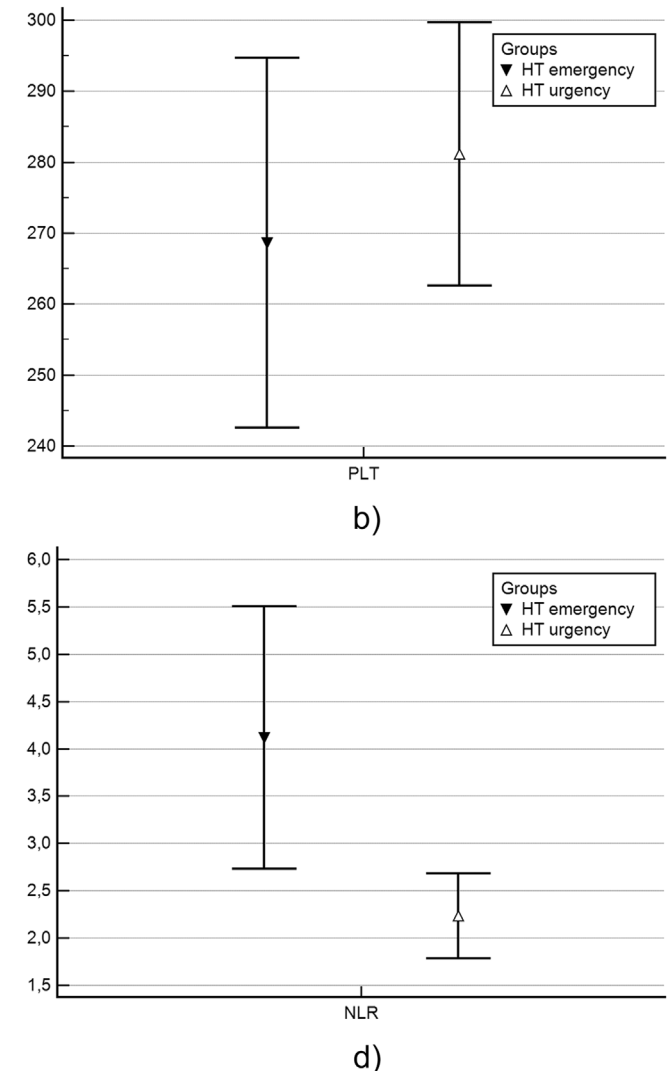


Fig. 2. Baseline characteristics of a) MPV b) PLT c) hs-CRP and d) NLR in geriatric patients with HT emergency urgency.

platelet count ($p = 0.434$).

An MPV level of 8.29 fL was found to be the best criterion value to discriminate between HT patients with end-organ damage or not with a sensitivity of 83.3% (95% CI: 69.8%–92.5%) specificity of 85.4% (95% CI: 72.2–93.9) and an accuracy of 0.92 (area under the curve (AUC) = 0.918, 95% CI: 0.844–0.964, $p < 0.001$; Fig. 3).

Pearson correlation analysis (Table 3) revealed positive but weak correlations between MPV and other variables.

4. Discussion

We found that mean MPV, hs-CRP level, NLR, and WBC count were higher in geriatric patients with HT emergencies compared to HT urgencies. Those parameters may play a role in the decision making and management of geriatric patients with HT emergencies.

MPV is increased in patients with diabetes mellitus, acute coronary syndrome, stroke, pre-eclampsia, renal artery stenosis, and hypercholesterolemia. Platelet parameters that can be easily measured aid in cardiovascular risk analysis (8, 9). Aging is accompanied by deterioration of arterial walls and the collagen of elastic tissue. These structural changes combine with increases in BP to accelerate the deterioration of vessel walls. Platelet activation and aggregation play important roles in the pathophysiology of atherosclerosis and cardiovascular morbidity and mortality in hypertensive patients (10). We confirmed that there is a slight relationship between the level of MPV (a measure of platelet function) and other inflammatory parameters that may play a role in acute cardiovascular events.

We also investigated the relationship between the clinical severity of HT and the level of MPV. Some studies found that hypertensive patients improved significantly when the increased platelet activation was treated, which is in parallel to the level of MPV (11). MPV was found to be an important marker of platelet activation in patients with obesity, acute MI, dyslipidemia, and HT (12, 13). Platelet activity increased in hypertensive patients, associated with a risk of organ damage (12). A significant correlation was evident between the MPV and the extent of microalbuminuria (a measure of subclinical end-organ damage) in patients with HT (14). Mean MPV was remarkably elevated in patients with HT compared with healthy controls or those with pre-HT (15). The principal finding of our study was that the average MPV was higher in geriatric patients with HT emergency (with end-organ damage) compared to those with HT urgency. An increased NLR and elevated platelet activity may trigger inflammation and thrombosis by increasing platelet adhesion to endothelial cells. By supporting this view, Gasparyan et al mentioned platelet activation as a link in the pathophysiology of diseases prone to thrombosis and inflammation (16).

We found that hs-CRP level, WBC count, and NLR were higher in patients with HT end-organ damage compared to HT urgencies. The levels of inflammatory parameters, including the WBC count and the hs-CRP level, were shown to be elevated in patients with unstable angina and acute MI (17). A relationship between inflammation and HT has also shown recently, but it is unclear whether inflammation is the cause or the result of the HT. However, an association was evident between a form of endothelial dysfunction and increased BP. The numbers of inflammatory cells in vessel walls are higher in hypertensive patients. As reflected in various guidelines, inflammatory biomarker levels usefully predict cardiovascular risks (18). A meta-analysis found that a higher NLR was associated with poorer functional outcomes and a higher risk of acute ischemic stroke (19). An increased NLR was strongly and independently associated with HT severity in patients with untreated essential HT and was reported as prognostically significant

regarding HT-associated complications such as heart failure and diseases of the CA, cerebral artery, and peripheral arteries (18).

In a study conducted by Ciftci et al., NLR was reported as an independent predictor of severe coronary disease of any degree with good sensitivity and moderate specificity (20). Moreover, Dorfell et al., found that levels of inflammatory biomarkers (IL-1 β and TNF- α) were higher in patients with HT than without HT (21). In another study, inflammatory parameters, including hs-CRP level, were higher in elderly patients with essential HT than in controls (22). Several recent studies have also shown that hs-CRP levels were higher in pre-HT patients compared with normotensive subjects, further supporting the relationship between HT and inflammation. We found no prior reports on any possible link between the inflammation and the clinical severity of patients experiencing hypertensive episodes. Therefore, any relationship between the severity of inflammation and acutely increased BP remains unclear. We explored the relationships between inflammatory markers such as NLR and hs-CRP level, and the severity of HT in geriatric patients admitted to our ED with HT attacks, and both parameters were significantly elevated in geriatric patients with HT emergencies rather than urgencies (23). Previous studies also revealed a clear link between the levels of hs-CRP and MPV. Those findings support the idea that end-organ disease caused by high BP is associated with increased platelet activity and inflammation. Thus, these parameters may reflect HT status and the risk of

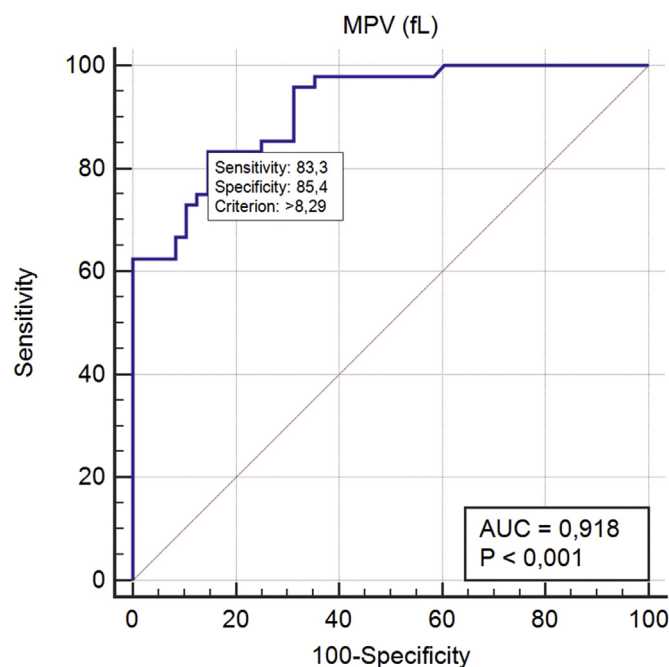


Fig. 3. The receiver operating characteristic (ROC) curve analysis of MPV for predicting HT emergencies.

Table 3
Correlation of MPV with other clinical and laboratory variables

| Variables | r | P |
|-----------------------------------|-------|--------|
| Hs-CRP (mg/dl) | 0.394 | <0.001 |
| WBC ($\times 10^3/\mu\text{l}$) | 0.362 | <0.001 |
| Troponin I (ng/ml) | 0.426 | <0.001 |
| SBP (mmHg) | 0.215 | 0.035 |
| NLR | 0.245 | 0.016 |

hs-CRP: high-sensitive C-reactive protein, MPV: mean platelet volume, SBP: systolic blood pressure, NLR: neutrophil-to-lymphocyte ratio, WBC: White blood cell count

organ damage in HT patients in the ED.

4.1. Study limitations

Our sample size was small. The study was performed in only one ED, and data were collected at only a single time point for evaluation of various parameters.

5. Conclusion

The mean MPV, hs-CRP, and NLR levels were higher in geriatric patients with HT emergency (with end-organ damage) compared to HT urgency. Furthermore, hs-CRP, NLR, and WBC counts were correlated with MPV levels as well. We conclude that end-organ damage in HT caused by high BP is associated with increased platelet activity and inflammation. Thus, these parameters may reflect HT status and the risk of organ damage in HT patients in the ED.

References

- Gulacti U, Lok U, Celik M, Aktas N, Polat H. The ED use and non-urgent visits of elderly patients. *Turkish Journal of Emergency Medicine*. 2016;16(4):141–145.
- Virdis A, Dell'Agnello U, Taddei S. Impact of inflammation on vascular disease in hypertension. *Maturitas*. 2014;78(4):179–183.
- Coppo M, Bandinelli M, Berni A, et al. Ang II Upregulation of the T-lymphocyte renin-angiotensin system is amplified by low-grade inflammation in human hypertension. *Am J Hypertens*. 2011;24(6):716–723.
- Sansanayudh N, Anothaisintawee T, Muntham D, McEvoy M, Attia J, Thakkinstian A. Mean platelet volume and coronary artery disease: a systematic review and meta analysis. *Int J Cardiol*. 2014;175(3):433–440.
- Karabacak M, Dogan A, Turkdogan AK, Kapci M, Duman A, Akpinar O. Mean platelet volume is increased in patients with hypertensive crises. *Platelets*. 2014;25(6):423–426.
- Mancia G, Fagard R, Narkiewicz K, et al. 2013 ESH/ESC Guidelines for the management of arterial hypertension: the task force for the management of arterial hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). *J Hypertens*. 2013;31:1281–1357.
- Varughese GI, Lip GY. Is hypertension a prothrombotic state? *Curr Hypertens Rep*. 2005;7(3):168–173.
- Ranjith MP, Raj RD, Mathew D, George B, Krishnan MN. Mean platelet volume and cardiovascular outcomes in acute myocardial infarction. *Heart Asia*. 2016 Feb 4;8(1):16–20.
- Du J, Wang Q, He B, et al. Association of mean platelet volume and platelet count with the development and prognosis of ischemic and hemorrhagic stroke. *Int J Lab Hematol*. 2016;38(3):233–239.
- Tsiara S, Elisaf M, Jagroop IA, et al. Platelets as predictors of vascular risk: is there a practical index of platelet activity? *Clin Appl Thromb Hemost*. 2003;9(3):177–190.
- Blann AD, Nadar S, Lip GYH. Pharmacological modulation of platelet function in hypertension. *Hypertension*. 2003;42(1):1–7.
- Park Y, Schoene N, Harris W. Mean platelet volume as an indicator of platelet activation: methodological issues. *Platelets*. 2002;13(5-6):301–306.
- Hekimsoy Z, Payzin B, Ornek T, Kandogan G. Mean platelet volume in Type 2 diabetic patients. *J Diabetes Complications*. 2004;18(3):173–176.
- Nadar SK, Blann AD, Kamath S, Beevers DG, Lip GY. Platelet indexes in relation to target organ damage in high-risk hypertensive patients: a substudy of the Anglo-Scandinavian Cardiac Outcomes Trial (ASCOT). *J Am Coll Cardiol*. 2004;44:415–422.
- Yarlioglus M, Kaya MC, Ardic I, et al. Relationship between Mean Platelet Volume Levels and Subclinical Target Organ Damage in Newly Diagnosed Hypertensive Patients. *Blood Press*; 2011:92–97 (2).
- Gasparyan AY, Ayyavazyan L, Mikhailidis DP, Kitis GD. Mean platelet volume: a link between thrombosis and inflammation? *Current Pharmaceutical Design*. 2011;17:47–58.
- Gokdemir MT, Kaya H, Sogut O, Kaya Z, Albayrak L, Taskın A. The role of oxidative stress and inflammation in the early evaluation of acute non-ST-elevation myocardial infarction: an observational study. *Anatol J Cardiol*. 2013;13(2):131–136.
- Hussain M, Saeed M, Babar MZM, Atif MA, Akhtar L. Nebivolol attenuates neutrophil lymphocyte ratio: a marker of subclinical inflammation in hypertensive patients. *International Journal of Hypertension*; 2017:6. Article ID 7643628 <https://doi.org/10.1155/2017/7643628>.
- Zhang J, Ren Q, Song Y, et al. Prognostic role of neutrophil-lymphocyte ratio in patients with acute ischemic stroke. *Medicine*. 2017;(e8624):10, 96:45.
- Ciftci O, Kayipmaz AE, Aydos TR, Muderrisoğlu IH. *Turkish Journal of Geriatrics*. 2017;20(1):8–16.
- Dörfel Y, Lätsch C, Stuhlmüller B, et al. Preactivated peripheral blood monocytes in patients with essential hypertension. *Hypertension*. 1999;34(1):113–117.
- Liu Q, Han L, Du Q, Zhang M, Zhou S, Shen X. The association between oxidative stress, activator protein-1, inflammatory, total antioxidant status and artery stiffness and the efficacy of olmesartan in elderly patients with mild-to-moderate essential hypertension. *Clin Exp Hypertens*. 2016;38(4):365–369.
- Ebong IA, Schreiner P, Lewis CE, Appiah D, Ghelani A, Wellons M. The association between high-sensitivity C-reactive protein and hypertension in women of the CARDIA study. *Menopause*. 2016;23(6):662–668.