The platelet-to-lymphocyte ratio as an inflammation marker in non-dipper hypertensive patients

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Abstract
Background: Non-dipper hypertensive patients have a higher risk of cardiovascular disease (CVD) than dipper hypertensive patients. Inflammation plays an important role in the pathogenesis and progression of CVD. This study aimed to determine the relationship between the platelet-to-lymphocyte ratio (PLR), and dipper and non-dipper hypertension.

Materials and Methods: This prospective study included 199 consecutive patients that were diagnosed with primary hypertension. According to ambulatory blood pressure monitoring measurements, non-dipper and dipper group were determined. PLR was determined based on the platelet count and lymphocyte count in the complete blood count.

Results: The non-dipper group included 103 patients (74 females and 29 males; mean age: 52.37 ± 10.7 years) and the dipper group included 96 patients (65 females and 31 males; mean age: 48.40 ± 11.1 years). Mean systolic blood pressure was significantly higher in the non-dipper group than in the dipper group (124 ± 15.1 mmHg versus 120 ± 11.2 mmHg, p = 0.032) and the median PLR was significantly higher in the non-dipper group than in the dipper group [132.15 (range: 69.64-400) versus 117.0 (range: 53.52-192.26), p = 0.001], whereas the mean white blood cell count (6.86 ± 1.43 × 10³/μL versus 7.24 ± 1.26 × 10³/μL, p = 0.046) and median lymphocyte count [2.09 (range: 0.95-3.92) × 10³/μL versus 2.24 (range: 0.97-3.98) × 10³/μL, p = 0.001] were significantly lower in the non-dipper group.

Conclusion: Median PLR was significantly higher in the non-dipper hypertensive patients than in the dipper hypertensive patients. We think this finding further supports the role of an increase in inflammatory response in non-dipper hypertension. Hippokratia 2015; 19 (2):114-118.

Keywords: Platelet-to-lymphocyte ratio, PLR, non-dipper hypertension, inflammation

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Introduction
Hypertension is a major cause of cardiovascular morbidity and mortality. Although its etiopathogenesis remains unclear, primary hypertension is thought to be closely associated with inflammation. Systolic and diastolic blood pressure are expected to drop >10% during the night, as compared to daytime, varying in accordance with circadian rhythm in normal and hypertensive individuals (dipper); in non-dipper hypertensive individuals systolic and diastolic blood pressure do not decrease. The risk of cardiovascular morbidity and mortality is higher in non-dipper hypertensive individuals, independent of mean blood pressure. This increased risk is suggested to be associated with the accelerated atherosclerotic process in non-dipper hypertensive individuals.

Inflammation is thought to play an important role in the pathogenesis of atherosclerotic cardiovascular disease (CVD). Such markers as high-sensitivity C-reactive protein (CRP), cytokines, matrix metalloproteinase-9, myeloperoxidase, intercellular adhesion molecule 1 (ICAM-1), soluble cluster of differentiation 40 (CD40) ligand, etc. have been reported to be indicative of inflammatory status. Indices derived from hemogram parameters have recently been defined as inflammatory markers, including the red cell distribution width (RDW), mean platelet volume (MPV), neutrophil-to-lymphocyte ratio (NLR), and platelet-to-lymphocyte ratio (PLR). PLR is the newest of these markers and was first studied in patients with malignancy. Subsequent research suggests that higher PLR is related with worse outcome in patients with atherosclerosis-related diseases, such as coronary artery disease (CAD) and heart valve diseases.
Peripheral arterial disease. The present study aimed to determine the relationship between PLR (as a marker of inflammation), and dipper and non-dipper hypertension.

Materials and Methods

This prospective study was conducted in an internal medicine clinic between May and December 2013, and included 199 consecutive patients diagnosed with primary hypertension. Demographic characteristics were recorded. All patients were assessed for cardiovascular risk factors (including smoking status, body mass index, cholesterol levels, duration of hypertension, medications used) and systemic diseases. Diabetes mellitus was defined as a new diagnosis according to 2011 American Diabetes Association (ADA) diagnostic criteria or receiving anti-diabetic therapy. Patients with diabetes mellitus, CAD, acute or chronic renal disease, secondary hypertension, cerebrovascular disease, acute or chronic infection, fever, collagen tissue disease, malignancy, hematological disease, thrombocytopenia (platelet count <150 x 10³ μL⁻¹), thrombocytosis (platelet count >450 x 10³ μL⁻¹), or use of anti-platelet, anti-coagulant, or immunosuppressive agents were excluded from the study.

Renal failure was defined according to the glomerular filtration rate (GFR), which was calculated using the simplified version of the Modification of Diet in Renal Disease study prediction equation formula, GFR=186 x Creatinine⁻¹·₄¹ x Age⁻₀·₂₀ x 1.212 (if African-American) x 0.742 (if female)²⁹. Patients diagnosed with chronic kidney disease were excluded according to the criteria defined by KDIGO (Kidney Disease Improving Global Outcomes) 2012 clinical practice guidelines for the evaluation and management of chronic kidney disease²⁹.

Infection and acute illness were determined based on the anamnesis and physical examination. Among the few patients with elevated CRP, in those in which clinical findings and symptoms were not consistent with acute illness, CRP was not interpreted in favor of infection or acute inflammation.

The 24-hour ambulatory blood pressure monitoring (ABPM) was performed using a WatchBP 03 device (Microlife WatchBP AG, Switzerland); the cuff was placed on the non-dominant arm. The devices were programmed to perform measurements every 15 min between 07:00 and 23:00 (daytime) and every 20 min between 23:00 and 07:00 (nighttime). The method was considered reliable if >70% of measurements were valid. Patients with a drop at night. There were no patients on more than two pills. All patients were taking antihypertensive agents; 112 were taking one pill, 61 were taking two drugs, and 11 were taking three drugs. All patients that were taking one drug, 61 were taking two drugs, and 11 were taking three drugs. All patients that were taking one pill (one drug or a fixed-dose combination of two drugs) took their pills in the morning; those that were taking two pills took one pill in the morning and the other 12 hours later at night. There were no patients on more than two pills.

Mean 24-hour SBP was significantly higher in the non-dipper group than in the dipper group (124 ± 15.1 mmHg versus 120 ± 11.2 mmHg, p=0.032) Mean asleep SBP was significantly higher in the non-dipper group than in the dipper group (119.25 ± 10.1 mmHg versus 113.28 ± 8.2 mmHg, p <0.001). Mean asleep DBP was significantly higher in the non-dipper group than in the dipper group (73.82 ± 6.56 mmHg versus 70.32 ± 7.2 mmHg, p <0.001) (Table 1). Among all patients, the mean creatinine levels were 0.8 ± 0.14 mg/dl; the mean white blood cell (WBC) count was 7.04 ± 1.36 x 10³/μL.
the median lymphocyte count was 2.18 (0.95-3.98) × 10³/μL; the mean platelet count was 279.7 ± 57.4 × 10³/μL, and the median PLR was 124 (53.5-400) (Table 2). The median PLR was significantly higher in the non-dipper group than in the dipper group [132.2 (69.6-400) versus 117.0 (53.5-192.3), p =0.001]. The WBC count was significantly lower in the non-dipper group than in the dipper group (6.86 ± 1.43 × 10³/μL versus 7.24 ± 1.26 × 10³/μL, p =0.046). Similarly, the lymphocyte count was significantly lower in the non-dipper group than in the dipper group [2.09 (0.95-3.92) × 10³/μL versus 2.24 (0.97-3.98) × 10³/μL, p =0.001) (Table 2).
Discussion

Non-dipper hypertension is considered an independent risk factor for all-cause mortality. Signs of renal platelet activity has been reported to correlate with an increase in the severity of inflammation. Increases in the platelet count, MPV, and RDW are indicators of increased platelet activity. Research has shown that a higher PLR in the absence of absolute thrombocytosis is associated with increased thrombosis and inflammation, which might be associated with an increase in platelet activity. Additionally, it was posited that relative lymphopenia in the presence of a high PLR might be indicative of the effect of an elevated endogenous cortisol level due to inflammatory response. Among a group of patients with obstructive peripheral artery disease, critical vascular stenosis and wounds due to vascular insufficiency were more common in those with a high PLR.

A study that examined the relationship between PLR and inflammation in cardiovascular diseases reported that a pre-procedural PLR >150, in patients diagnosed with ST segment elevation myocardial infarction that underwent primary percutaneous coronary stent placement, was predictive of no-reflow, with sensitivity of 75% and specificity of 74%.

In the present study, the PLR (used as a marker of inflammation) was significantly higher in the non-dipper hypertension group than in the dipper hypertension group. Moreover, PLR was found to be an independent predictive factor. A PLR of 101.5 or higher predicted non-dipper status with 84.5% sensitivity and 39.6% specificity. The fact that both of the present study’s patient groups were similar in terms of smoking status, body mass index, cholesterol levels, duration of hypertension, medications used, and lack of other known chronic diseases strengthens the validity of the findings. Furthermore, the present findings are similar to those of an earlier relevant study that reported the PLR was significantly higher in non-dipper hypertensive patients, a PLR ≥107 was predictive of non-dipper hypertension (with sensitivity of 66.3% and specificity of 68.7%), and that NLR and hs-CRP levels were higher in non-dipper hypertension group. Although specificity of PLR cutoff value was low our study, the values were similar.

Table 3: Significant predictors of non-dipper pattern in hypertensive patients.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Odds Ratio</th>
<th>lower</th>
<th>Upper</th>
</tr>
</thead>
<tbody>
<tr>
<td>24 h- mean SBP</td>
<td>1.027</td>
<td>1.012</td>
<td>1.051</td>
</tr>
<tr>
<td>PLR</td>
<td>1.014</td>
<td>1.010</td>
<td>1.022</td>
</tr>
</tbody>
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p <0.05 is considered significant for statistical analyses, SBP: systolic blood pressure, PLR: platelet-to-lymphocyte ratio, CI: confidence intervals.
level on the prognosis of hypertension. In conclusion, the present findings suggest that the PLR can be used in daily practice as a marker of inflammation because it is easy to calculate using hemogram parameters and is a cost-effective index. The present study also shows that a high PLR might be indicative of high atherosclerotic risk in hypertensive patients and a predictive value can be determined in the future.

Conflict of Interest Statement
The authors report no conflicts of interest, financial or otherwise.

References