# The relation between monocyte/HDL-cholesterol ratio and dipper/non-dipper blood pressure status in patients with newly diagnosed hypertension

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#### Abstract

**Aim:** In this study, It was ivestigated to see if there was a correlation between dipper and non-dipper hypertension conditions and the MHR in patients newly diagnosed with hypertension.

**Material and Methods:** One hundred and thirty-nine newly diagnosed hypertension patients who admitted department of cardiology. Patients were divided into two groups; dipper group and non-dipper group and Monocyte/HDL-cholesterol Ratio, high sensitive-C reactive protein and dipper/non-dipper status were examined.

**Results:** There were 61 patients (mean age 47±13 and 48% male) in the dipper group and 78 patients (mean age 52±12and 49% male) in the non-dipper group. Mean MHR was 0.01550±0.00447 in dipper group and 0.01810±0.00661 in non-dipper group. Mean MHR was significantly higher in non-dipper group (0.009). There was a significant and positive correlation between MHR and Hs-CRP (r=0.350; p<0.001).

**Conclusion:** When compared to the patients newly diagnosed with dipper hypertension, it has a high MHR level in the group of patients with non-dipper hypertension.

Keywords: Dippers; hypertension; monocyte-to-high-density lipoprotein ratio; non-dippers

# INTRODUCTION

Cardiovascular diseases are the most common reason for mortality and morbidity across the world. Uncontrolled hypertension is one of the most important alterable cardiovascular risk factors. Blood pressure (BP) undergoes circadian changes throughout the day. The circadian difference obtained from blood pressure measurements with ambulatory blood pressure monitoring (ABPM) is associated with cardiovascular prognosis. When compared with daytime BP measurements in ambulatory blood pressure measurements, 10% or higher decrease in nighttime BP measurements are defined as per "dipper," whereas do not show a decrease is defined as "nondipper" (1). It has been shown in studies that the absence of a decrease or the presence of an increase in nighttime BP compared to the daytime BP measurements is an independent risk factor for cardiovascular diseases (2,3).

Inflammation and lipid accumulation are some of the main features of atherosclerosis, and both conditions have been found to be associated with hypertension (4,5).

It has been shown in previous studies that high monocyte count and low high density lipoprotein (HDL)-cholesterol levels are associated with inflammation and oxidative stress, while monocyte/HDL ratio (MHR) is associated with hypertension and other cardiovascular diseases (6-10).

With this overview, we investigated in this study to see there was a correlation between dipper and non-dipper hypertension conditions and the MHR in patients newly diagnosed with hypertension.

# **MATERIAL and METHODS**

### **Study population**

One hundred and thirty nine newly diagnosed hypertension patients who admitted department of Cardiology in Kayseri City Hospital were enrolled in study from March 2018 to February 2019. If the systolic BP (SBP) was greater than 140 mm Hg and/or the diastolic BP (DBP) was greater than 90 mm Hg was determined hypertension (1). After the initial assessment, blood samples were taken from all patients and ABPM was placed on patients

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for at least 24 hours to assess blood pressure. History of heart failure, history of coronary artery disease that documented with angiography, history of chronic and acute renal disease (or serum creatinine level > 1.5 mg/ dL), anemia, clinical evidence of active infection, active malignancy, hematological proliferative diseases, active or chronic inflammatory or autoimmune diseases, pregnancy, recent blood transfusion and patients with secondary hypertension were excluded from the study. The research was conducted in accordance with the principles of the Declaration of Helsinki. Approval for the study was acquired from the local ethics committee.

#### **Ambulatory Blood Pressure Assessment**

ABPM was recorded by the tonoport V (Ge Healthcare, California, U.S.A) oscillometric monitoring device. Daytime were measured every 15 minutes and nighttime systolic and diastolic blood pressures were measured every 30 minutes for 24 hour period in all patients. The recordings were studied using interactive software. If daytime systolic blood pressure decreased at least 10% or more at nighttime was accepted 'dipper' and all other patients were accepted 'non-dipper'. According to this definition, patients were divided into two groups; dipper group and non-dipper group.

#### Laboratory analyzes

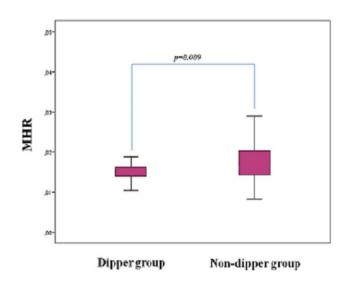
Antecubital venous blood samples for laboratory analysis were drawn for routine hypertension assessment after patients had fasted for 10 h. Glucose, creatinine, lipid profile and common blood count parameters were analyzed using an autoanalyzer. High sensitive C reactive protein (Hs-CRP) was measured using a BN2 model nephelometer. MHR was calculated as the ratio of the monocyte count to the level of HDL.

#### **Statistical Analysis**

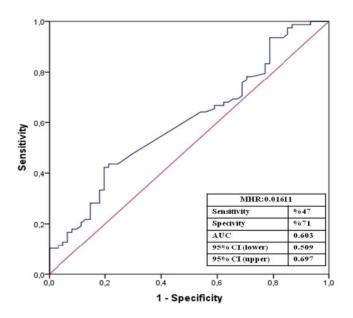
Kolmogorov-Smirnov test was used to test continuous variables for normal distribution. We report continuous data as mean and standard deviation or median. Continuous variables were analyzed by using the Student t-test or Mann-Whitney U test between groups. Categorical variables were summed up as percentages and compared with the Chi-square test. The association between MHR/Hs-CRP values and MHR/nocturnal fall in systolic BP were evaluated by calculating the Pearson correlation coefficient. A two-sided p value < 0.05 was considered statistically significant. All data analysis was performed using the Statistical Package for the Social Sciences version 22 (SPPS-22).

## RESULTS

There were 61 patients (mean age  $47\pm13$  and 48% male) in the dipper group and 78 patients (mean age  $52\pm12$  and 49%male) in the non-dipper group. Baseline characteristics are shown in Table 1. Mean age was significantly higher in the non-dipper group ( $52\pm12$ , p=0.012). There were no significant differences in the sex, diabetes mellitus, current smoking and body mass index between groups. Laboratory parameters also are shown in Table 1. The monocyte levels of patient significantly higher in the non-dipper group ( $0.65\pm0.14$  vs  $0.72\pm0.17$ , p=0.009). Hs-CRP levels of patient significantly higher in the non-dipper group ( $2.64\pm1.26$  vs  $3.54\pm1.87$ , p=0.002). Mean MHR was  $0.01550\pm0.00447$  in dipper group and  $0.01810\pm0.00661$ in non-dipper group. Mean MHR was significantly higher in non-dipper group (p=0.009) (Figure 1). The receiver operating characteristics analysis for MHR in predicting non-dipper hypertension is shown in Figure 2. A MHR > 0.01611 had a 47% sensitivity and 71% specificity in predicting non-dipper hypertension. There was a significant and positive correlation between MHR and Hs-CRP (r=0.350; p<0.001) (Figure 3). Other parameters in laboratory analysis did not differ between into two groups (Table 1).



**Figure 1.** MHR between dipper and non-dipper group. MHR: Monocyte/HDL ratio



**Figure 2.** Receiver operating characteristic curve of MHR. AUC: Area under curve, MHR: Monocyte/HDL ratio

Table 1. Comparison of baseline characteristics and laboratory parameters of the study groups				
	Dipper group n=61	Non-dipper group n=78	p value	
Age (year)	47±13	52±12	0.012	
Sex (male)	29 (48%)	38 (49%)	0.890	
Diabetes mellitus (%)	20 (33%)	21 (27%)	0.452	
Current smoker (%)	22 (36%)	25 (32%)	0.620	
BMI (kg/m²)	26.91±2.67	26.44±2.90	0.334	
Hemoglobin (g/l)	14.67±1.77	14.38±1.74	0.332	
Platelet (/mm3)	278±69	278±80	0.989	
WBC (10^3/µl)	8.53±2.13	8.79±2.33	0.506	
Neutrophil (10^3/µl)	4.92±1.59	5.33±1.92	0.176	
Lymphocyte (10^3/µl)	2.73±0.67	2.56±0.77	0.170	
Monocyte (10^3/µl)	0.65±0.14	0.72±0.17	0.009	
Glucose (mg/dL)	104±30	113±48	0.182	
Creatinine (mg/dL)	0.86±0.24	0.88±0.25	0.646	
LDL-C (mg/dL)	111±22	115±24	0.249	
HDL-C (mg/dL)	43.43±7.41	41.78±8.12	0.219	
Total cholesterol (mg/dL)	188±25	192±30	0.435	
Triglycerides (mg/dL)	188±69	197±82	0.468	
Hs-CRP (mg/l)	2.64±1.26	3.54±1.87	0.002	
MHR	0.01550±0.00447	0.01810±0.00661	0.009	

Data are expressed as mean ± SD or median for normally distributed data and percentage (%) for categorical variables

Table 2. Comparison of ABPM results between groups				
	Dipper group n=61	Non-dipper group n=78	p value	
Clinical SBP, mm Hg	142.9±12.2	145.9±14.1	0.179	
Clinical DBP, mm Hg	89.3±5.1	88.5±5.1	0.379	
Mean daytime SBP, mm Hg	155.9±12.4	154.6±10.4	0.486	
Mean daytime DBP, mm Hg	94.5±11.5	92.9±9.7	0.377	
Mean nighttime SBP, mm Hg	134.9±11.1	152.7±12.6	<0.001	
Mean nighttime DBP, mm Hg	77.9±9.9	87.6±10.4	<0.001	
Mean 24-hour SBP, mm Hg	147.9±11.3	153.9±10.2	0.001	
Mean 24-hour DBP, mm Hg	87.9±10.6	91.0±9.4	0.069	
Nocturnal fall in SBP, %	13.5±3.8	5.1±3.9	<0.001	
Nocturnal fall in DBP, %	17.8±5.1	7.2±5.6	<0.001	

Data are expressed as mean ± SD or median for normally distributed data. SBP. Sistolic blood pressure, DBP. Diastolic blood pressure, ABPM: Ambulatory blood pressure monitoring

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Comparison of ABPM results between groups are shown in Table 2. Mean nighttime SBP (134.9±11.1 vs 152.7±12.6, p<0.001), Mean nighttime DBP (77.9±9.9 vs 87.6±10.4, p<0.001) and Mean 24-hour SBP (147.9±11.3 vs 153.9±10.2, p=0.001) were significantly higher in non-dipper group. As expected, nocturnal fall in SBP and in DBP were significantly higher in the dipper group (13.5±3.8 vs 5.1±3.9, p<0.001 and 17.8±5.1 vs 7.2±5.6, p<0.001 respectively). Clinical SBP, Clinical DBP, Mean daytime SBP, Mean daytime DBP and Mean 24-hour DBP were similar between groups.

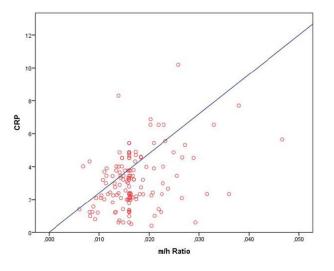


Figure 3. Correlation between Hs-CRP and MHR

# DISCUSSION

We evaluated association between MHR and dipper/nondipper status in newly diagnosed hypertension patients. We found significantly higher MHR in patients with nondipper group and also were found significantly positive but weak correlation between Hs-CRP- acute inflammation marker- and MHR.

Hypertension is one of the most important reasons for mortality and morbidity around the world (11). When the pathophysiology of hypertension is studied; endothelial damage and dysfunction, inflammation, oxidative stress and coagulation disorders can be said to be among the causes. Elevated systolic and diastolic blood pressures are independent predictive risk factors for cardiovascular diseases (1). Under normal conditions, blood pressure shows a circadian rhythm. Nighttime decrease in both systolic and diastolic blood pressure values is a physiological condition. It has been shown in studies that when compared with daytime blood pressure measurements conducted with ABPM, the absence of a 10% or higher decrease in nighttime blood pressure measurements is closely associated with deteriorated cardiovascular conditions and deteriorated target organ damage (12-14). Even though increased vascular resistance and increased nighttime sympathetic nervous system activity are said to be associated with non-dipper hypertension, the underlying reason is still unclear (15).

It has been shown in previous studies that nondipper hypertension is also associated with increased inflammation (16-18). Monocyte cells are cells that are found in the peripheral blood and have their own specific roles in the inflammatory response. Monocytes play a significant role in the progression of atherosclerosis (19). Additionally, an inflammatory and procoagulant condition arises by means of the tissue factors released from circulating monocytes and this inflammatory process is said to be associated with cardiovascular diseases (20). Unlike this process, HDL cholesterol reduces the monocyte uptake of the monocyte in the arterial wall and cuts down on the detrimental effects of the monocyte, therefore protects endothelial cells from inflammation and oxidative stress. (6,21,22). A correlation between increased MHR and cardiovascular diseases, familial mediterranean fever, chronic renal failure, metabolic syndrome and diseases with underlying chronic inflammation such as macular degeneration has been indicated in recent studies (11,23-28). In addition, in the study conducted by Aydın et al, a significant correlation has been found between MHR and hypertension-related asymptomatic organ damage (8).

There are studies performed on the correlation between dipper and non-dipper hypertension and inflammatory indicators (29-32). Studies typically focus on increased inflammation in patients with non-dipper hypertension. Endothelial dysfunction and procoagulant condition have been found to be associated with increased cardiovascular conditions due to increased inflammatory load caused by non-dipper hypertension. In our study in which we examined the correlation between dipper and non-dipper hypertension, a significant correlation has also been found with increased CRP levels, which is an indicator of inflammation. As MHR is an inexpensive and easily accessible biomarker, it will be a guide for patients following a hypertension treatment.

The biggest limitation of our study is that it is a single center study with a small number of patients and it is designed as a cross sectional study. The non-dipper group consisted of significantly older patients may have affected the monocyte / HDL ratio is another limitation in our study. There is a need for prospective randomized follow-up studies with a bigger number of patients.

# CONCLUSION

In conclusion, when compared to the patients newly diagnosed with dipper hypertension, it has a high MHR level in the group of patients with non-dipper hypertension. Still, studies to investigate the correlation between MHR and prognosis with treatment methods to be followed in large patient populations are required.

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