



Red cell distribution width, leukocyte and neutrophil counts in patients with non-dipper hypertension, dippers and normotensives

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ARTICLE INFO

ABSTRACT

Article History

Received 13 / 07 / 2014

Accepted 20 / 08 / 2014

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Both non-dipping hypertension and high red blood distribution width (RDW) values are associated with adverse cardiovascular events and inflammatory status in cardiovascular disease and the general population. Thus, in this study we investigated relationship between RDW and non-dipping hypertension compared with normotensives. A total of 907 participants were included in the study. The nocturnal decline in blood pressure is by less than 10% of the daytime value has been termed non-dippers. According to the values of ambulatory BP, the patients were divided into three groups as non-dipper hypertensive (n=246), dipper hypertensive (n=250), and normotensive (n=411) ones. There were no significant differences among groups regarding baseline demographic properties and biochemical characteristics. Non-dipper and dipper hypertensive groups had higher leukocyte and neutrophil counts than normotensive group ($p<0.001$) but the leukocyte and neutrophil counts did not differ between the hypertensive groups. There was no difference in RDW levels among non-dipper, dipper and normotensives (13.3(22.8-11.2), 13.1(22.8-11.2), 13.1(19.2-11), $p=0.53$, respectively). RDW level was not associated with dipper and non-dipper hypertension. There was a positive correlation between the RDW level and neutrophil counts and systolic blood pressure but the correlation was weak.

J. Exp. Clin. Med., 2014; 31:155-159

Keywords:

Dippers
Leukocyte
Neutrophil
Non-dipper hypertension
Red cell distribution

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1. Introduction

Arterial blood pressure (BP) exhibits a diurnal rhythm that is higher in daytime than at nighttime (Richardson et al., 1964; Millar-Craig et al., 1978). Patients with a nocturnal decline in blood pressure of less than 10% of the daytime value have been termed non-dippers (Ayala et al., 2009). Continuous 24-h ambulatory blood pressure monitoring (ABP) has been used to show the diurnal rhythm of arterial blood pressure. Previous studies have shown that non-dipper hypertension (HT) is related to adverse cardiovascular events, severe renal dysfunction, and cerebrovascular disease (Ohkubo et al., 1997; Kario et al., 2001; Davidson et al., 2006). Although the

causes of non-dipper hypertension are not fully understood, mechanisms like volume expansion and increased sympathetic activity have been postulated previously (Nakano et al., 2001). Also it was reported that non-dipper hypertension was associated with inflammatory status (Kaya et al., 2010).

Red cell distribution width (RDW) is a marker of variability in terms of size of circulating erythrocytes. It is routinely used as a component of automated complete blood count (CBC) in clinical practice. Recent studies have indicated that there is a strong association between elevated RDW levels and mortality in patients with coronary artery disease (Tonelli et al., 2008; Patel et al., 2009; Perlstein et al

2009). Lappe et al. (2011) demonstrated that high-sensitivity C-reactive protein (hsCRP) was strongly associated with RDW in patients with coronary artery disease (CAD). In another study it was found that elevated RDW levels might reflect enhanced erythropoiesis resulting from elevated circulating levels of neurohumoral mediators (Kato et al., 2005). Also in a few studies with smaller patient numbers RDW levels was increased in patients with hypertension and non-dipper hypertension (Gunebakmaz et al., 2012; Tanındı et al., 2012; Ozcan et al., 2013). Thus, we aimed to evaluate whether there is a difference between RDW levels and leukocyte count in non-dipper hypertensive patients compared to dipper hypertensive patients and to non-hypertensive.

2. Experimental procedure

Patients and methods

In our cross-sectional study, a total of 2500 patients, between the ages of 18 and 80 years, were evaluated with ABP monitoring between January 2011 and December 2012 in our cardiology outpatient clinic. Subjects in control group were chosen from our outpatient clinic that has no cardiovascular and significant systemic disease. Medical history, physical examination results, and anthropometric measurements were taken from the medical records of these groups. Any deficient, missing or unavailable data in terms of blood count results on admission resulted in the exclusion of related patients. By the end of the recruitment process, 907 patients remained and were included in the study.

HT was defined as having an office blood pressure (OBP) of $\geq 140/90$ mm Hg, daytime ABP of $\geq 135/85$ mm Hg, or the active use of antihypertensive drugs. Non-hypertension was defined as having a consistent normal BP on OBP and daytime ABP measurements in patients not receiving active antihypertensive treatment (OBP $< 140/90$ mm Hg and daytime ABP $< 135/85$ mm Hg) (O'Brien et al., 2005). Non-dippers were defined as those with nocturnal decrease in either systolic blood pressure (SBP) or diastolic blood pressure of less than 10% of daytime (Ayala et al., 2009). Patients were divided into three groups according to ambulatory BP values and OBP, respectively, non-dipper hypertensive (n=246), dipper hypertensive (n=250), and non-hypertensive (n=411).

Diabetes was defined based on the American Diabetes Association guideline criteria such as fasting serum glucose of ≥ 126 mg/dL (7 mmol/L), or nonfasting glucose of ≥ 200 mg/dL (11.1 mmol/L), or active use antidiabetic treatment (Expert Committee on the diagnosis and Classification of diabetes mellitus., 2003). Body mass index was calculated as (weight in kilograms)/(height in meters)². The exclusion criteria of this study were the presence of secondary hypertension, heart failure, coronary artery disease, stroke, moderate to severe valvular disease, chronic renal failure, chronic liver disease, thromboembolic disorders, hematological abnormalities and chronic obstructive pulmonary disease. The patients having a total leukocyte count of > 12.000 , neutrophil count of $> 78\%$, lymphocyte count of $> 63\%$, or monocyte count of $> 14\%$, since extreme levels could represent occult diseases were also excluded. Informed consent was obtained from all patients, and the Local Ethics Committee approved the study protocol.

Ambulatory blood pressure monitoring

Ambulatory blood pressure monitoring (ABPM) was

performed for 24-h using an ambulatory BP monitor (Tonoport V, GE Healthcare). The monitor was programmed to measure BP every 15 min from 08:00 to 20:00 and every 30 min from 20:00 to 08:00. Daytime and nighttime BP was defined from 07:00 to 23:00 h for daytime and from 23:00 to 07:00 for nighttime respectively.

Red cell distribution width

RDW was measured in blood samples collected in EDTA tubes, which were analyzed with an automated hematology analysis system (Mindray BC5800). Normal RDW values ranged from 11- to 16% in our laboratory. Standard laboratory parameters, including total leukocyte, neutrophil count, hematocrit, glucose, creatinine, and lipid profiles were determined with standard methods.

Statistics

Statistical analyses were performed using the SPSS software version 17. The variables were investigated using visual (histograms, probability plots) and analytical methods (Kolmogorov-Smirnov) to determine whether they were normally distributed. Descriptive analyses were presented using means and standard deviations (SD) for normally distributed, using medians and maximum-minimum for the non-normally distributed and categorical variables were expressed as percentages. Groups were compared with one-way analysis of variance (ANOVA; age, total cholesterol, low-density lipid [LDL]-cholesterol, body mass index, hematocrit), the Kruskal-Wallis test, and the Chi-Square test. Comparisons of non-parametric values among groups were performed by the Kruskal Wallis test. Mann-Whitney U-test (for non-parametric variables) with Bonferroni adjustment were used for multiple comparisons between the groups. P value of less than 0.017 was considered to be significant in Bonferroni adjustment. A Spearman correlation analysis was performed to determine the association of RDW with neutrophil count, leukocyte count, 24-h SBP, 24-h diastolic blood pressure (DBP), 24-h mean arterial blood pressure (MABP), and night SBP-DBP in all groups. An overall 5% type-I error level was used to infer statistical significance.

3. Results

There were no difference between patient and control groups regarding baseline demographic and biochemical characteristics. The percentage of antihypertensive medications was similar between dipper and non-dipper groups. Body mass index (BMI) was lower in the control group (27 ± 6 kg/m²) than that in the non-dipper (31 ± 4 kg/m²) and dipper (30 ± 5 kg/m²) groups, but the difference was not statistically significant ($p=0.328$). Although the non-dipper and dipper hypertensive groups had higher leukocyte and neutrophil counts than those in the non-hypertensive group ($p<0.001$), the leukocyte and neutrophil counts did not show any difference between hypertensive groups. RDW level was higher in non-dipper hypertensive group than that in dipper and non-hypertensive group but there was no statistically significant difference among non-dipper, dipper, and non-hypertensive groups in terms of RDW levels 13.3(22.8-11.2), 13.1(22.8-11.2), 13.1(19.2-11) respectively, ($p=0.531$) (Table 1).

While the nighttime SBP and DBP in the non-dipper group (154 ± 15 , 92 ± 10 mmHg) were higher than those in the

Table 1. Characteristics of the study population

	Non-dippers (n=246)	Dippers (n=250)	Normotensives (n=411)	p-value
	mean±SD or median (minimum-maximum)	mean±SD or median (minimum-maximum)	mean±SD or median (minimum-maximum)	
Gender(male) n, (%)	125(50.8)	117(46.8)	187(45.5)	0.411
Age, years	55±12	53±12	52±13	0.610
BMI, kg/m ²	31±4	30±5	27±6	0.328
Diabetes, (%)	52 (21.1)	51(20.4)	67(16.3)	0.225
Glucose, mg/dl	97 (73-140.5)	99 (78-132)	97 (72-198)	0.156
Creatinine, mg/dl	0.8(1.1-0.5)	0.8(1.3-0.5)	0.8(1.3-0.5)	0.109
Total-cholesterol, mg/dl	203±43	205±44	203±40	0.775
LDL, mg/dl	134±33	132±37	131±35	0.621
HDL-cholesterol, mg/dl	45(22-101)	45(19-97)	47(23-106)	0.060
Triglycerides, mg/dl	138(49-350)	132(18-465)	137(26-608)	0.969
Hematocrit, %	42±5	42±4	41±4	0.121
Neutrophill, x 10³/mm³	4.4(9.6-1.7)	4.5(9.7-1.6)	3.9(7.8-0.5)*	<0.001
Leukocyte, x 10³/mm³	7.7(14 - 4.1)	7.4(15.2 - 3.6)	6.9(13.1-3.1)*	<0.001
RDW, %	13.3 (22.8 -11.2)	13.1(22.8 -11.2)	13.1(19.2-11)	0.531
ACE inh.use, (%)	20.5	(23.4)		0.743
ARB use, (%)	14.7	16		0.540
Beta-blocker use, (%)	11.7	9		0.350
CCB use, (%)	17.6	11.8		0.103
Diuretic use, (%)	18.6	21.4		0.820

ACE: Angiotensin-converting enzyme; ARB: Angiotensin receptor blocker; CCB: Ca-channel blocker; BMI: Body mass index; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; LDL: Low-density lipoprotein; HDL: High-density lipoprotein; RDW: Red blood distribution width; *p<0.01 non-dipper and dipper vs non-hypertensive group. * P value of less than 0.017 was considered to be significant in Bonferroni adjustment among the groups.

dipper group (141±112, 82±9 mmHg) (p<0.001), the daytime SBP and DBP in the dipper group (156±10.97±10 mmHg) were higher as compared to non-dipper group (154±13, 94±11 mmHg, p<0.001, p=0.002). Twenty-four hours SBP, 24-h DBP and 24-h MABP were similar between these groups (Table 2). While there was a weak positive correlation between the RDW level and neutrophil counts between two groups, there was no correlation between RDW level and leukocyte count, (r=0.126, p<0.001 and r=0.017, p=0.610, respectively). Also, there was weak positive correlation between RDW and 24-SBP, 24- MABP, day SBP and night SBP (Table 3).

Table 2. Comparison of the ambulatory blood pressure monitoring variables among two groups

Blood pressure (mmHg)	Non-dippers	Dippers	p-value
Daytime-SBP	154±13	156±10	0.002
Daytime-DBP	94±11	97±10	<0.001
Nighttime-SBP	154±15	141±12	<0.001
Nighttime-DBP	92±10	82±9	<0.001
24-h-SBP	154±12	152±14	0.266
24-h-DBP	93±10	94±9	0.542
24-h MAB	124±10	123±10	0.735

SBP: Systolic blood pressure; DBP: Diastolic blood pressure; MAB: mean arterial blood pressure

4. Discussion

Three important findings emerged from this study. First, the RDW levels did not show any difference between hypertensive and normotensive groups. Second RDW level was not associated with dipping pattern in hypertensive patients. Third, the leukocyte and neutrophil counts of hypertensive patients were higher than normotensive, but the leukocyte and neutrophil counts did not differ between non-dipper and dipper groups.

RDW is a measure of the variation in the size of erythrocytes, and higher values reflect a more heterogeneous red cell population. Hemolysis, nutritional deficiencies, including iron, vitamin B12, and folate, blood transfusion, thrombotic thrombocytopenic purpura, and inflammatory bowel diseases can cause increased RDW levels (Evans and Jehle, 1991; Perkins, 2003). In clinical practice, RDW is usually used for differential diagnosis of microcytic anemia (McKenzie, 2003). Recent studies showed that higher RDW levels are associated with increased mortality in patients with heart failure and CAD (Felker et al., 2007; Fukuta et al., 2009). In addition, several community-based studies observed that higher RDW values were related with increased risk of mortality in general population (Patel et al., 2009; Perlstein et al., 2009). Perlstein et al. (2009) assessed 15.852 adult participants of the Third National Health and Nutrition Examination Survey and found that higher RDW levels were strongly associated with risk of all-cause, cardiovascular disease mortality. RDW levels are influenced by multiple conditions. Hemolysis, nutritional deficiencies, including iron, vitamin B12, and folate, in addition to inflammation and oxidative stress might lead to elevated RDW levels by not only impairing iron metabolism but also by suppressing the production of erythropoietin or by reducing red blood cell survival (Douglas and Adamson, 1975; Tozzi-Ciancarelli et al., 1989; Manabe et al., 2005; Weiss and Goodnough 2005; Marinkovic et al., 2007).

Although it was demonstrated, by Sozmen et al. (1998) that both hypertension and RDW level were associated with inflammation and oxidative stress, we did not find any relationship between RDW level and hypertension in our study. This may be due to several reasons. First, RDW level is determined by many conditions like inflammation and oxidative stress. In the NHANES III study, the association of RDW with mortality risk did not entirely depend upon

Table 3. Correlations between selected covariates and RDW

	r	p-value
24-h diastolic blood pressure	0.045	0.172
24-h systolic blood pressure	0.089	0.070
24-h Mean blood pressure	0.045	0.025
Day systolic blood pressure	0.073	0.029
Day diastolic blood pressure	0.034	0.320
Night systolic blood pressure	0.101	0.002
Night diastolic blood pressure	0.69	0.038
Neutrophil count	0.126	<0.001
Leukocyte count	0.017	0.061

inflammation (Perlstein et al., 2009). There was no difference in the risk estimate for RDW in patients with elevated CRP compared to those with low CRP in the NHANES III study. In addition, Fukuta et al. (2009) did not find a relationship between hsCRP and RDW levels in patients with CAD. In contrast to our study, Wen (2010) reported that high RDW was strongly and independently associated with intimal medial thickness and the incidence of carotid plaque in patients with hypertension. Also, in another cross-sectional study involving 217,567 Spanish working-age individuals undergoing a routine medical checkup, it was found that increased RDW is related to metabolic syndrome (MetS) (Sánchez-Chaparro et al., 2010). Above two study populations probably had high cardiovascular disease burden, which is reflected in more severe inflammation and oxidative stress. Intensity of inflammation and oxidative stress may not be enough to affect RDW levels in patients with hypertension who are otherwise healthy in our study.

In our study, although it did not reach statistical significance, RDW levels were higher in hypertensive patients than normotensive ($p=0.531$). Moreover, contrary to our study there are small studies reporting that RDW levels were higher in hypertensive patients compared to prehypertensive and healthy subjects. (Mean RDW levels were 16.54 ± 0.91 , 15.26 ± 0.82 , and 13.87 ± 0.94 in hypertensive, prehypertensive, and control groups, respectively ($p<0.05$) (Tanındı et al., 2012). In contrast to a study by Tanındı et al. (2012) which revealed that mean RDW level was above the upper normal limits (RDW<15) in hypertensive patients our study revealed that mean RDW level was significantly lower in the hypertensive patients. We could not explain the reason for this difference but may be due to different study populations. There is only few small studies in the literature to show the higher RDW levels in non-dipper hypertensives compared to dipper hypertensive (Gunebakmaz et al., 2012; Ozcan et al., 2013). In contrast to these studies, we could not demonstrate any relation between RDW levels and non-dipping pattern in hypertensive patients. There are numerous factors such as

follic acid; B12 vitamin and iron deficiency could be affecting RDW levels. It seems that these studies did not take into consideration of these potential factors influencing RDW levels. The reason of these conflicting results in different studies including relationship of RDW, hypertension and non dipping pattern might be caused by these factors explained above.

Studies have indicated that SBP has a greater association with RDW than does diastolic blood pressure (DBP) (Tonelli et al., 2008; Patel et al., 2009). While we detected a positive correlation between 24-hour SBP and RDW, we could not detect an association between DBP and RDW. Systolic hypertension has also been shown to be more closely associated with increased inflammation and NT-proBNP than is diastolic hypertension (Pusuroğlu et al., 2014a; Pusuroğlu et al., 2014b). This may explain the different associations of RDW with SBP and DBP.

White blood cell (WBC) and neutrophil counts are simple but effective markers of chronic inflammation (Marinkovic et al., 2007). Some studies have reported that markers of systemic low-grade inflammation and oxidative stress are increased in patients with hypertension (Portaluppi et al., 2004; Pauletto and Rattazzi, 2006). In present study neutrophil and leukocyte counts were higher in hypertensive group than in normotensive group. In small sample study by Demir (2013) it was reported that neutrophil and leukocyte counts were higher in non-dipper hypertensive patients than in dipper hypertensive patients whereas we found that neutrophil and leukocyte counts did not differ among hypertensive groups.

Limitations

There are several limitations in this study. First, this study is subject to the limitations of retrospective design. Second, the study population consisted of hypertensive population without heart failure, coronary artery disease, stroke, and moderate to severe vascular disease. Thus, our finding cannot be generalized to all of the hypertensive population. Third, we did not measure vitamin B12 or folate levels and iron status, which may affect RDW levels. Fourth, we did not detect high sensitivity C-reactive protein, B-type natriuretic peptides, and other neurohumoral mediators that provide valuable clues regarding the mechanism underlying anisocytosis.

5. Conclusion

We found that RDW levels were similar in hypertensive and normotensive groups. Also RDW was not associated with non-dipping pattern in patients with hypertension. However, larger studies are needed to assess the exact role of RDW level in hypertensive patients.

REFERENCES

- Ayala, D.E., Hermida, R.C., Chayan, L., Mojon, A., Fontao, M.J., Fernandez, J.R., 2009. Circadian pattern of ambulatory blood pressure in untreated hypertensive patients with and without metabolic syndrome. *Chronobiol. Int.* 26, 1189-1205.
- Davidson, M.B., Hix, J.K., Vidt, D.G., Brotman, D.J., 2006. Association of impaired diurnal blood pressure variation with a subsequent decline in glomerular filtration rate. *Arch. Intern. Med.* 166, 846-852.
- Demir, M., 2013. The relationship between neutrophil/lymphocyte ratio and non-dipper hypertension. *Hytens.* 35:5703. doi:10.3109/10641963.2013.764893.
- Douglas, S.W., Adamson, J.W., 1975. The anemia of chronic disorders: Studies of marrow regulation and iron metabolism. *Blood.* 45, 55-65.
- Evans, T.C., Jehle, D., 1991. The red blood cell distribution width. *J. Emerg. Med.* 9, 71-74.
- Expert Committee on the Diagnosis and Classification of Diabetes Mellitus., 2003. Report of the expert committee on the diagnosis and

- classification of diabetes mellitus. *Diabetes Care*. 26, 5-20.
- Felker, G.M., Allen, L.A., Pocock, S.J., Shaw, L.K., McMurray, J.J., Pfeffer, M.A., Swedberg, K., Wang, D., Yusuf, S., Michelson, E.L., Granger, C.B., CHARM Investigators, 2007. Red cell distribution width as a novel prognostic marker in heart failure: Data from the CHARM Program and the Duke Databank. *J. Am. Coll. Cardiol.* 50, 40-47.
- Fukuta, H., Ohte, N., Mukai, S., Saeki, T., Asada, K., Wakami, K., Kimura G., 2009. Elevated plasma levels of B-type natriuretic peptide but not C-reactive protein are associated with higher red cell distribution width in patients with coronary artery disease. *Int. Heart. J.* 50, 301-312.
- Gunbakmaz, O., Kaya, M.G., Duran, M., Akpek, M., Elcik, D., Eryol, N.K., 2012. Red blood cell distribution width in “non-dipper” versus “dippers.” *Cardiology*. 123, 154-159.
- Kario, K., Pickering, T.G., Matsuo, T., Hoshida, S., Schwartz, J.E., Shimada, K., 2001. Stroke prognosis and abnormal nocturnal blood pressure falls in older hypertensives. *Hypertension*. 38, 852-857.
- Kato, H., Ishida, J., Imagawa, S., Saito, T., Suzuki, N., Matsuoka, T., Sugaya, T., Tanimoto, K., Yokoo, T., Ohneda, O., Sugiyama, F., Yagami, K., Fujita, T., Yamamoto, M., Nangaku, M., Fukamizu, A., 2005. Enhanced erythropoiesis mediated by activation of the renin-angiotensin system via angiotensin II type 1a receptor. *FASEB*. 19, 2023-2025.
- Kaya, M.G., Yarlioglu, M., Gunbakmaz, O., Gunturk, E., Inanc, T., Dogan, A., Kalay, N., Topsakal, R., 2010. Platelet activation and inflammatory response in patients with non-dipper hypertension. *Atherosclerosis*. 209, 278-282.
- Lappé, J.M., Horne, B.D., Shah, S.H., May, H.T., Muhlestein, J.B., Lappé, D.L., 2011. Red cell distribution width, C-reactive protein, the complete blood count, and mortality in patients with coronary disease and a normal comparison population. *Clin. Chim. Acta.* 412, 2094-2099.
- Manabe, S., Okura, T., Watanabe, S., Higaki, J., 2005. Association between carotid haemodynamics and inflammation in patients with essential hypertension. *J. Hum. Hypertens.* 19, 787-791.
- Marinkovic, D., Zhang, X., Yalcin, S., Luciano, J.P., Bruynars, C., Huber, T., Ghaffari, S., 2007. Foxo3 is required for the regulation of oxidative stress in erythropoiesis. *J. Clin. Invest.* 117, 2133-2144.
- McKenzie, S.D., 2003. Introduction to anemia. In: McKenzie, S.D., (Editor). *Clinical laboratory hematology*. Saddle River, NJ: Pearson Prentice-Hall. pp. 161-188.
- Millar-Craig, N.W., Bishop, C.V., Raftery, E.B., 1978. Circadian variation of blood pressure. *Lancet* 11, 795-797
- Nakano, Y., Oshima, T., Ozono, R., Higashi, Y., Sasaki, S., Matsumoto, T., Matsuura H, Chayama K, Kambe M., 2001. Non-dipper phenomenon in essential hypertension is related to blunted nocturnal rise and fall of sympathovagal nervous activity and progress in retinopathy. *Auto Neurosci*. 2001. 14, 181-186.
- O'Brien, E., Asmar, R., Beilin, L., Imai, Y., Mancia, G., Mengden, T., Myers M., Padfield P., Palatini P., Parati G., Pickering T., Redon J., Staessen J., Stergiou G., Verdecchia P., 2005. European Society of Hypertension Working Group on Blood Pressure Monitoring. Practice guidelines of the European Society of Hypertension for clinic, ambulatory and self-blood pressure measurement. *J Hypertens*. 23:697-701.
- Ohkubo, T., Imai, Y., Tsuji, I., Nagai, K., Watanabe, N., Minami, N., Kato, J., Kikuchi, N., Nishiyama, A., Aihara, A., Sekino, M., Satoh, H., Hisamichi, S., 1997. Relation between nocturnal decline in blood pressure and mortality. The Ohasama Study. *Am. J. Hypertens.* 10, 1201-1207.
- Ozcan, F., Turak, O., Durak, A., İşleyen, A., Uçar, F., Giniş, Z., Uçar, F., Başar, F.N., Aydoğdu, S., 2013. Red cell distribution width and inflammation in patients with non-dipper hypertension. *Blood Press*. 22, 80-85.
- Patel, K.V., Ferrucci, L., Ershler, W.B., Longo, D.L., Guralnik, J.M., 2009. Red blood cell distribution width and the risk of death in middle-aged and older adults. *Arch. Intern. Med.* 169, 515-523.
- Pauletto, P., Rattazzi, M., 2006. Inflammation and hypertension: The search for a link. *Nephrol. Dial. Transplant*. 21, 850-853.
- Perkins, S.L., 2003. *Wintrobe's Clinical Hematology*. 11th ed. Salt Lake City, UT, Lippincott Wilkins & Williams pp. 5-25.
- Perlstein, T.S., Weuve, J., Pfeffer, M.A., Beckman, J.A., 2009. Red blood cell distribution width and mortality risk in a community-based prospective cohort. *Arch. Intern. Med.* 169, 588-594.
- Portaluppi, F., Boari, B., Manfredini, R., 2004. Oxidative stress in essential hypertension. *Current Pharma. Design*. 10, 1695-1698.
- Pusuroglu, H., Erturk, M., Akgul, A., Surgit, O., Çelik, O., Demir, A., Ozal, E., Bolat, I., Çakmak, H., Ozdoğan, O., Uyarel, H., Uslu, Nevza., 2014 b. Plasma N-Terminal Pro-Brain Natriuretic Peptide Levels Identifying Non-Dipping Pattern in Patients with Hypertension. *Exp Clin Cardiol.* 20, 64-85.
- Pusuroglu, H., Akgul, A., Erturk, M., Ozal, E., Celik, O., Gül, M., Surgit, O., Oner, E., Akturk, F., Birant, A., Cakmak, H.A., Uslu, N., 2014 a. A comparative analysis of leukocyte and leukocyte subtype counts among isolated systolic hypertensive, systo-diastolic hypertensive and nonhypertensive patients. *Kardiol Pol* . doi: 10.5603/KP.a2014.0044
- Richardson, D.W., Honour, A.J., Fenton, G.W., Scott, F.H., Pickering, G.W., 1964. Variation in arterial pressure throughout the day and night. *Clin Sci*. 26, 445-460.
- Sánchez-Chaparro, M.A., Calvo-Bonacho, E., González-Quintela, A., Cabrera, M., Sáinz, J.C., Fernández-Labandera, C., Aguado, L.Q., Meseguer, A.F., Valdivielso, P., RománGarcía, J., Ibermutuamur cardiovascular risk Assessment Study Group., 2010. Higher red blood cell distribution width is associated with the metabolic syndrome: results of the Ibermutuamur Cardiovascular Risk assessment study. *Diabetes Care*. 33, 40. doi:10.2337/dc09-1707.
- Sözmen, B., Kazaz, C., Taşkıran, D., Arslan, L., Akyol, A., Yıldırım Sözmen, E., 1998. Plazma antioksidant status and nitrate levels in patients with hypertension and coronary heart disease. *Tr. J. Medical Sciences* 28, 525-531.
- Tanırdı, A., Topal, F.E., Topal, F., Celik, B., 2012. Red cell distribution width in patients prehypertension and hypertension. *Blood Press*. 21, 177-181. doi:10.3109/08037051.2012.645335.
- Tonelli, M., Sacks, F., Arnold, M., Moye, L., Davis, B., Pfeffer, M., 2008. Relation between red blood cell distribution width and cardio-vascular event rate in people with coronary disease. *Circulation*. 117, 163-168.
- Tozzi-Ciancarelli, M.G., Di Giulio, A., Troiani-Sevi, E., D'Alfonso, A., Amicosante, G., Oratore, A., 1989. Human erythrocyte damage at the initial stages of oxidative stress. *Cell Biophys*. 15, 225-234.
- Weiss, G., Goodnough, L., 2005. Anemia of chronic disease. *N. Engl. J. Med.* 352, 1011-1123.
- Wen, Y., 2010. High red blood cell distribution width is closely associated with risk of carotid artery atherosclerosis in patients with hypertension. *Exp. Clin. Cardiol.* 15, 37-40.