ORIGINAL RESEARCH PAPER

Medicine

CORRELATION OF DIPPER AND NON DIPPER STATUS WITH LEFT VENTRICULAR DIASTOLIC DYSFUNCTION IN OBESE PATIENTS

KEY WORDS: ABPM- Ambulatory blood pressure monitoring
ECHO- Echocardiography

Ritesh Yadav	Junior Resident, Dept Of Medicine, command hospital (western command) Panchkula, Haryana
Navreet Singh*	MD (MED) , DM(CARDIO), Dept Of Medicine, command hospital (western command) Panchkula, Haryana *Corresponding Auhtor
Dr. Anil Kumar	MD (MED) , DM(CARDIO), Dept Of Medicine, command hospital (western command) Panchkula, Haryana *Corresponding Auhtor
Abhinav Tiwari	Junior Resident, Dept Of Medicine, command hospital (western command) Panchkula, Haryana *Corresponding Auhtor
Neeraj Kumar	Junior Resident, Dept Of Medicine, command hospital (western command) Panchkula, Haryana *Corresponding Auhtor
Inderpal	Junior Resident, Dept Of Medicine, command hospital (western command) Panchkula, Haryana *Corresponding Auhtor

ABSTRACT

Ambulatory blood pressure monitoring (ABPM) correlates better with target organ damage than office blood pressure monitoring. Non dipping status on ABPM, defined as <10% dip in night time BP and is considered as a marker of adverse cardiovascular prognosis.

The study evaluated the presence of LV diastolic dysfunction in obese patients and correlates it with DIPPER v/s NON DIPPER status and the prevalence of non-dippers in obese patients.

RESULTS: Out of the total 31 patients under study total of 71% (n=28) were found to be dippers. Test of one proportion was used to analyse the significance of proportion of patients with dipper and non-dipper status in the study. The Z statistic came out to be 2.338(95% confidence interval; 52% to85.5%) which was found to be significant at p=0.0194 level of confidence.

CONCLUSION: there is a positive correlation between presence of diastolic dysfunction and obesity with non-dipping status on ABPM.

INTRODUCTION

DEFINITION OF OBESITY

INDIAN GUIDELINES:

Three simple measures of obesity are widely used in clinical practice; body mass index (BMI), waist circumference (WC) and waist-to-hip circumference ratio (WHR). The most widely used method is BMI

Consensus Statement

a. BMI is the most researched measure of generalized obesity and should continue to be used using Asian Indian-specific cut-offs as described later.
b. Waist circumference should be used as a measure of abdominal obesity with Asian Indian specific cut-offs.
c. Both BMI and WC should be used together (with equal importance) for population- and clinic-based metabolic and cardiovascular risk stratification.
   Consensus Statement (1)
   Normal BMI: 18.0-22.9 kg/m2 , Overweight: 23.0-24.9 kg/ m2 , Obesity: >25 kg/m2

PREVALENCE

In India, obesity is emerging as an important health problem particularly in urban areas, paradoxically co-existing with under nutrition. 51.3% of adult urban Indians are obese. (2)

DIASTOLIC DYSFUNCTION

Diastolic dysfunction refers to when the diastole part of this action is abnormal. The ventricles do not properly relax and become stiff meaning they cannot fill with blood properly. This causes blood to "dam up" in other parts of the body.

The diagnosis of HF can be performed obviously by the simple clinical examination but the identification of the diastolic origin needs an instrumental assessment. DD may be asymptomatic and, therefore, identified occasionally during a Doppler echocardiographic examination.

AMBULATORY BLOOD PRESSURE MONITORING

Since Riva-Rocci (3) invented the sphygmomanometer in 1886, casual blood pressure measurement has been used for the assessment of blood pressure and its control. However, the value of casual blood pressure is questionable in all its contexts in the last five decades.

Since the study published by Aiman & Goldshine in 1940,(4) it has been known that a significant percentage of patients have higher blood pressure measures when they are taken in the clinic setting than at home. In addition, blood pressure measures taken by doctors are usually higher. (5)

This development has changed the paradigm of the best method to assess blood pressure behaviour. The ambulatory blood pressure monitoring (ABPM) is the method of choice for 24 hour-blood pressure monitoring considering its advantages established in previous reviews and guidelines. (6, 7)

Thresholds for Hypertension Diagnosis Based on ABPM (8)

24-h Average	≥130/80 mm Hg
Awake (daytime) average	≥135/85 mm Hg
Asleep (night-time) average	≥120/70 mm Hg

DAY/NIGHT BP CYCLE

Day and night variability of BP has been shown by means of non-invasive ambulatory BP monitoring (9)

DIPPERS AND NON DIPPERS

O'Brien et Al (10) and Pickering (11) originally proposed to classify subjects as nondippers or dippers according to the magnitude of their nocturnal hypotension. Nondippers and dippers individuals can be classified with a fall of mean night-time BP <10% and ≥10% than the average daytime values, respectively. Evidence that the nondipping phenomenon is prognostically adverse has grown in a consistent fashion. (12, 13)

DIPPER STATUS AMONG OBESE PATIENTS

Obese, but otherwise healthy, individuals are at higher risk of reduced nocturnal BP dipping (14) compared with normal-weight peers.

IMPORTANCE OF THIS STUDY

Obese patients are predisposed to cardiovascular complications; one of early prognostic parameter for same would be LV diastolic dysfunction. This study will review the evidence on the prognostic value of ambulatory BP. After this study we establish the prognostic value of dipper and nondipper status as an early indicator of future cardiovascular complications. All this may have important implications for the treatment strategies to be adopted as well as for the appreciation of the protective effect of the prescribed therapy making a case for routine use of ABPM in management of HTN and cardiovascular patients.

AIMS AND OBJECTIVES

1. To study the presence of LV diastolic dysfunction in patients under study and correlate it with their DIPPER v/s NON DIPPER status

MATERIALS AND METHODS

The study is a cross sectional study carried out at Command Hospital (Western Command) Chandimandir Panchkula, Haryana on patients referred to or coming directly to this hospital who meet the inclusion criteria.

METHOD OF COLLECTION OF DATA:

INCLUSION CRITERIA:

1. Patients between ages of 18 to 65 years.
2. BMI of more than 25
3. Not on any pharmacological treatment for diastolic dysfunction

EXCLUSION CRITERIA:

1. Taking treatment for diastolic dysfunction
2. Case of Hypertrophic cardiomyopathy, aortic stenosis, restrictive heart disease.
3. Pregnant and nursing patients
4. Children below the age of 18 years and adults above the age of 65 years.
5. Patients with BMI below 25
6. Ischemic heart disease
7. Valvular heart disease
9. Patients who do not give consent to be a part of the study.

PROCEDURE

LV Diastolic dysfunction would be established, by 2D Echocardiography (ECHO MACHINE DETAILS: GE Vivid Pro S/W DIAGNOSTIC ULTRASOUND SYSTEM, CLASSA, GROUP 1, SN: 613397WXO GE MEDICAL SYSTEMS (CHINA) CO.LTD) for these patients will be accessed by dedicated cardiologist and findings will be recorded. Those who classify as obese and have diastolic dysfunction will be screened for dipper and non-dipper status by ABPM. The 24 hour ambulatory BP will be noted (ABPM MACHINE DETAILS: SCHILLER, TYPE BRT02 PLUS. S/N: 290.0970. BAAR SWITZERLAND**)**. The data will be shown in terms of numbers and percentages. And the data will be analyzed by appropriate statistical tools.

24 hour ABPM procedure:

- Day time considered from 0700 hrs. to 2100 hrs. Night period considered from 2100 hrs. to 0700 hrs.
- Blood pressure readings will be taken every 30 minutes.
- The monitor should then be placed in the pouch and secured on a belt (provide if required) around the waist.
- Instruct patient to keep a relaxed arm and not to talk whilst readings are being taken and that if a reading is not obtained, the machine will take it again after 5 minutes. Inform the patient that if they are driving and the cuff inflates to ignore it until they can pull over safely. If the monitor does not obtain the reading then it will repeat the process after 5 minutes. Instruct the patient not to get the monitor wet.
- Upload monitor onto computer using standard software and print.

According to the 2D echocardiographic findings, the patients would be classified according to the grades of diastolic dysfunction. There would be 4 grades of diastolic dysfunction:

1. Grade 1: mild diastolic dysfunction (impaired LV relaxation). Mitral Inflow: E/A ≤0.75. Mitral Inflow at Peak Valsalva Maneuver : E/A <0.5. Doppler tissue imaging of mitral annular motion. E/e' < 10.
2. Grade 2: moderate diastolic dysfunction (pseudo normal). Mitral Inflow: 0.75< E/A <1.5, DT >140 msec.. Mitral Inflow At Peak Valsalva Maneuver E/A ≥0.5. . Doppler tissue imaging of mitral annular motion. E/e' ≥ 10.
3. Grade 3: severe diastolic dysfunction (reversible restrictive). Mitral Inflow: E/A ≥1.5, DT <140 msec. Mitral Inflow At Peak Valsalva Maneuver E/A ≥0.5. . Doppler tissue imaging of mitral annular motion. E/e' ≥ 10.
4. Grade 4: severe diastolic dysfunction(fixed restrictive). Mitral Inflow: E/A >1.5, DT <140 msec. Mitral Inflow At Peak Valsalva Maneuver E/A <0.5. . Doppler tissue imaging of mitral annular motion. E/e' ≥ 10.

RESULTS AND ANALYSIS:

The data was tabulated in Microsoft Excel and was analysed by the SPSS V23 software. The nature of data was studied using mean and standard deviation for quantitative variable and frequency distribution for qualitative variables. The comparison of the categorical variables was done by applying Pearson Chi-Square Test. A p-value of < 0.05 was considered as statistically significant. Test of one proportion was used to analyse the final result.

RESULT AND OBSERVATION

The present study was conducted to study the correlation between LV Diastolic dysfunction and dipper and non-dipper status among obese patients. In present study, a total of 31 obese patients with diastolic dysfunction were enrolled. Sampling method used was simple random sampling. The study has shown the following results. The values are expressed as percentages and mean ± SD (Standard deviation).

Demography profile of the patients

The demographic profile of the participants in this study is given in table 1 and 2. When demographic characteristics of the sample analysed, the calculated mean age of the participants was found to be 40.23±8.65 years. Mean weight of participants was 95.48±8.28 Kilograms and mean height was 172.23±6.16 centimetres. The calculated mean Body mass index (BMI) was 32.17±2.25.

Table 1

Sex	Frequency	Percent
Female	3	9.7%
Male	28	90.3%
Total	31	100.0%

Table 2

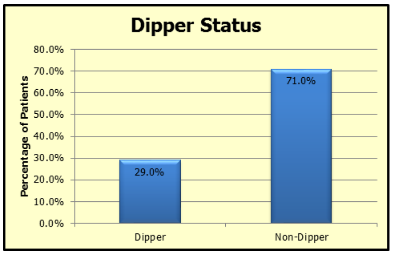
Descriptive Statistics						
	N	Minimum	Maximum	Mean		Std. Deviation
	Statistic	Statistic	Statistic	Statistic	Std. Error	Statistic
Age	31	24	63	40.23	1.555	8.659
Height	31	151	180	172.23	1.107	6.163
Weight	31	71	108	95.48	1.488	8.286
BMI	31	28.34	40.50	32.1732	.40530	2.25663

Distribution of dipper and non-dipper patients in study

The distribution of dipper and non-dipper patients is given in table 3. Total of 29% of participants had a dipper status (n=9), and 71% had a non-dipper status (n=71%)

Table 3

Dipper	Frequency	Percent
Dipper	9	29.0%
Non-Dipper	22	71.0%
Total	31	100.0%



Comparison of demographic profile among the dipper and non-dipper patients

Comparison of demographic profile between various demographic parameters is as per table 4 and 5. The mean age of dipper is 39.89 years and non-dipper is 40.36. Average height in dipper and non-dipper is 174.11 cm and 171.45 cm respectively. Mean BMI for dipper is 32.332, and for non-dipper is 32.1082 respectively. The 'p' value for age, height weight and bmi is 0.893, 0.283, o.376 and 0.807 none of which is significant (p>0.05 for all). Both the groups are comparable, with no apparent selection bias.

Table 4

Dipper Status Final		N	Mean	Std. Deviation	Std. Error Mean
Age	Dipper	9	39.89	6.173	2.058
	Non-dipper	22	40.36	9.619	2.051
Height	Dipper	9	174.11	5.011	1.670
	Non-dipper	22	171.45	6.523	1.391
Weight	Dipper	8	97.63	8.070	2.853
	Non-dipper	22	94.50	8.523	1.817
BMI	Dipper	9	32.3322	1.67906	.55969
	Non-dipper	22	32.1082	2.48708	.53025

Table 5

	t	df	Sig. (2tailed)	Mean Difference	Std. Error Difference	95%Confidence Interval of the Difference	
						Lower	Upper
Age	-.136	29	.893	-.475	3.484	-7.600	6.650
Height	1.093	29	.283	2.657	2.431	-2.315	7.628
Weight	.900	28	.376	3.125	3.473	-3.989	10.239
BMI	.247	29	.807	.22404	.90722	-1.63144	2.07952

Distribution of lab parameters within the dipper and non dipper groups

The distribution of lab parameters between dipper and non-dipper group is given in table 6. The 'p' value for all the lab values as per table 7 is more than 0.05, that is all the lab parameters within the 2 groups are comparable with no selection bias, only exception being serum cholesterol with a 'p' value of 0.028 is significant. I.e. serum cholesterol may be a confounding factor among the lab parameters.

Table 6

Dipper Status Final		N	Mean	Std. Deviation	Std. Error Mean
HB	Dipper	9	14.211	1.2098	.4033
	Non-dipper	22	14.491	1.2735	.2715
TLC	Dipper	9	6111.11	1131.862	377.287
	Non-dipper	22	6990.91	1326.617	282.836
Platelet	Dipper	9	325666.67	61619.802	20539.934
	Non-dipper	22	317636.36	95016.563	20257.599
Bl. Urea	Dipper	9	27.00	8.031	2.677
	Non-dipper	22	31.27	7.199	1.535
S. Creatinine	Dipper	9	.911	.1167	.0389
	Non-dipper	22	.882	.2281	.0486
Na+	Dipper	9	142.56	3.644	1.215
	Non-dipper	22	141.82	3.825	.816
K+	Dipper	9	3.867	.1936	.0645
	Non-dipper	22	3.795	.2319	.0494

Dipper Status Final		N	Mean	Std. Deviation	Std. Error Mean
Sr. Cholesterol	Dipper	9	206.78	35.379	11.793
	Non-dipper	22	181.82	23.321	4.972
Sr. Triglycerides	Dipper	9	180.33	46.052	15.351
	Non-dipper	22	183.82	60.906	12.985
HDL	Dipper	9	52.33	6.910	2.303
	Non-dipper	22	51.95	9.327	1.989
LDL	Dipper	9	120.11	20.251	6.750
	Non-dipper	22	111.18	14.595	3.112
PT(t)	Dipper	9	13.33	.500	.167
	Non-dipper	22	13.36	.581	.124
PT©	Dipper	9	13.00	0.000	0.000
	Non-dipper	22	13.09	.294	.063
INR	Dipper	9	1.02	.044	.015
	Non-dipper	22	1.01	.047	.010
BSL	Dipper	9	88.67	9.260	3.087
	Non-dipper	22	103.05	46.407	9.894

Table 7

	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	95% Confidence Interval of the Difference	
HB	-.563	29	.578	-.2798	.4971	-1.2964	.7368
TLC	-1.743	29	.092	-879.798	504.839	-1912.309	152.713
Platelet	.233	29	.817	8030.303	34461.018	-62450.393	78510.999
Bl. Urea	-1.452	29	.157	-4.273	2.943	-10.292	1.747
S. Creatinine	.364	29	.719	.0293	.0805	-.1354	.1940
Na+	.494	29	.625	.737	1.494	-2.318	3.793
K+	.811	29	.424	.0712	.0879	-.1085	.2509
Sr. Cholesterol	2.320	29	.028	24.960	10.757	2.958	46.961
Sr. Triglycerides	-.154	29	.879	-3.485	22.631	-49.771	42.801
HDL	.110	29	.913	.379	3.453	-6.684	7.442
LDL	1.380	29	.178	8.929	6.470	-4.304	22.162
PT(t)	-.137	29	.892	-.030	.222	-.483	.423
PT(c)	-.918	29	.366	-.091	.099	-.294	.112
INR	.471	29	.641	.009	.018	-.029	.046
BSL	-.913	29	.369	-14.379	15.744	-46.578	17.821

Comparison of 2D Echo findings within Dipper and non-dipper groups

The mean e/a value in dipper and non-dipper groups are 1.72 and 1.52 respectively. It's more than 1.5 in both the groups showing presence of diastolic dysfunction. And the e/e' value in dipper and non-dipper groups is 22.32 and 13.36 respectively as depicted in table 8. It's more than 10 in both the groups showing presence of diastolic dysfunction. The 'p' value for the entire echo values as per table 9 is more than 0.05 that is all the lab parameters within the 2 groups are comparable with no selection bias.

Table 8

Dipper Status Final		N	Mean	Std. Deviation	Std. Error Mean
E	Dipper	9	1.0289	.14348	.04783
	Non-dipper	22	.9982	.19627	.04184
A	Dipper	9	.6200	.10607	.03536
	Non-dipper	22	.7177	.25368	.05408
e'	Dipper	9	.07056	.040654	.013551
	Non-dipper	22	.08000	.029921	.006379
e/a	Dipper	9	1.72236	.523402	.174467
	Non-dipper	22	1.53762	.562187	.119859
e/e'	Dipper	9	22.3218	19.73326	6.57775
	Non-dipper	22	13.3613	3.09606	.66008

Table 9

	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	95% Confidence Interval of the Difference	
E	.424	29	.675	.03071	.07250	-.11757	.17899
A	-1.512	28.920	.141	-.09773	.06461	-.22990	.03444
e'	-.718	29	.478	-.009444	.013148	-.036336	.017447
e/a	.846	29	.404	.184743	.218323	-.261777	.631263
e/e'	1.355	8.162	.212	8.96058	6.61079	-6.23154	24.15269

Analysis of results as per test for one proportion

Analysis of the results is given as per table 10. All the patients included in the study after satisfying the selection criteria were essentially obese and had diastolic dysfunction also. We did their ambulatory BP measurement, to see for the dipper and non-dipper status and further analysed the results. Test of one proportion was used to analyse the significance of proportion of patients with dipper and non-dipper status in the study. The Z statistic came out to be 2.338(95% confidence interval; 52% to85.5%) which was found to be significant at p=0.0194 level of confidence.

Table 10

Data	
Observed proportion (%)	71
Sample size	31
Null Hypothesis value (%)	50

Results

The results showed that the Z statistic came out to be 2.338(95% confidence interval; 52% to85.5%) which was found to be significant at p=0.0194 level of confidence. The results are tabulated in table 11.

Table 11

Results	
95% CI of observed proportion	52% to 85.8%
z statistic	2.338
Significance level	P = 0.0194*

*Significant

DISCUSSION

The present study was conducted to study the correlation between LV Diastolic dysfunction and dipper and non-dipper status among obese patients.

Non-dipping status has been shown to have significant effects on health outcomes. In adults, specifically, non-dipping has been associated with poor cardiovascular, (15, 16) renal, (17) and diabetic outcomes (18). Nocturnal hypertension and non-dipping have been associated in adolescent diabetics with diabetic nephropathy, (19) LVH, (20). Non-dipping has also been associated with worsening GFR in children with CKD. (21) .

This is the first study, as concluded after thorough internet search, which correlates non-dipper status on ABPM monitoring among obese patients with diastolic dysfunction. As non-dipper state is a strong indicator (15, 16, 17, 18) of poor cardiovascular renal and diabetic outcomes. We intend to establish the prognostic value of ABPM in this subset i.e. to say that this subset would require intensive management and close follow-up.

Patients of both genders of the age between 18-65 years were included in the study. The mean age of the patients was 40.23 yrs., which was found to be lesser than the mean age in a similar study (22). The difference may be due to selective bias of young serving combatants, which are the primary patients in this hospital

In our study 90.3% were males (n=28), and 9.7% were females(n=3). This is there because of selection bias for combatants.

According to our study out of the total study subjects who were all having diastolic dysfunction and were obese, total 71%(n=22) were non-dipper while 29%(n=22) were dipper. The prevalence of non-dipper in obese patients was found to be 71%. As compared to Ian R Macumber et all who found this prevalence to be 34.4%,(23) our prevalence was much higher, this is likely due to a selection bias of selecting patients with diastolic dysfunction which in itself is an adverse prognostic marker.

According to our study after using test for one proportion it was analysed that non-dipper percentage was 71%. A significant proportion of the sample was non-dipper as concluded from a p value of 0.0194(p<0.05). That implies that diastolic dysfunction in obese patients has a positive correlation with non-dipping status, and hence non-dipping status can be accepted as a valid marker of high risk for cardiac disorders. Diastolic dysfunction is a marker of underlying cardiac illness(24), namely congestive heart failure, coronary artery disease, hypertension, sudden cardiac death to name a few. This prognosticates that non-dipper obese have poor outcome cardiologically.

According to Cuspidi C et al and Hermida RC AD et al, non-dipping status is associated with poor cardiovascular outcome(15,16) . Further according to Redfield MM JS et al, diastolic dysfunction independently is a marker of poor cardiological outcome (24). Both these combined would likely be more powerful predictors than either of them independently i.e if both these are present in a patient then such individuals would be at a highest risk of developing cardiovascular events than with either of them alone and this necessitates more aggressively management of modifiable cardiological risk factors.

Our data also further support the benefit of utilizing ABPM in the evaluation of hypertension, as it offers valuable information that cannot be ascertained from office or home BP measurements.

Limitations of the study

Because of the study being non-prospective, the causality cannot be established

Dipping and non-dipping status are also dependent on sodium intake and exercise habits of the patient, which we have not considered.

The small sample size prevents us from generalisation of the results.

CONCLUSION

Our study concluded that there is a positive correlation between presence of diastolic dysfunction and obesity with non-dipping status on ABPM. This provides a basis for further prospective study into this relationship, as well as adds to the public health importance of non-dipping status.

As non-dipping are so clearly linked to worse health outcomes in adults, it is important for us to continue to describe the relationship between obesity, diastolic dysfunction and non-dipping, as well as continue to investigate health outcomes in this subset. And since there is high likelihood of increased adverse outcome in this subset, hence the need for early and aggressive management in them is warranted.

We however hypothesize that non-dipper status is an early indicator of future cardiovascular diseases in obese patients. All this may have important implications for the treatment strategies to be adopted as well as for the appreciation of the protective effect of the prescribed therapy making a case for routine use of ABPM in management of HTN and cardiovascular patients.

REFERENCES

1. http://www.japi.org/february_2009/R-1.pdf IcSAf.
2. Undavalli VK, Ponnaganti SC, Narni H. Prevalence of generalized and abdominal obesity: India's big problem. Int J Community Med Public Health 2018;5:1311-6.
3. Riva-Rocci S. Um nuovo sfigmomanometro. Gazz Med Torino. 1896;47:981-1001.
4. Ayman D, Goldshine AD. Blood pressure determinations by patients with essential hypertension. Am J Med Sci. 1940;200:465-74.
5. Pierin AM, Souza V, Lima JC, Mano GM, Ortega K, Ignęs EC, et al. White coat effect and white coat hypertension and office blood pressure measurement taken by patients, nurses, and doctors compared with ambulatory blood pressure monitoring. J Hypertens. 2002;20(4 Suppl):S975.
6. O Brien E, Parati G, Stergiou G. Ambulatory Blood Pressure Measurement: what Is the international consensus? Hypertension. 2013;62(6):988-94.
7. Parati G, Stergiou G, O Brien E, Asmar R, Beilin L, Bilo G, et al; European Society of Hypertension Working Group on Blood Pressure Monitoring and Cardiovascular Variability. European Society of Hypertension practice guidelines for ambulatory blood pressure monitoring. J Hypertens. 2014;32(7):1359-66.
8. Chobanian A, Bakris G, Black H, Cushman W, Green L, Izzo J et al. Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. Hypertension. 2003;42(6):1206-1252.
9. Pickering T. Recommendations for the use of home (self) and ambulatory blood pressure monitoring. American Society of Hypertension Ad Hoc Panel. Am J Hypertens. 1996;9:1–11.
10. O Brien E, Sheridan J, O Malley K. Dippers and non-dippers. Lancet. 1988;2:397.
11. Pickering TG. The clinical significance of diurnal blood pressure variations. Dippers and nondippers. Circulation. 1990;81:700–702.
12. Rizzoni D, Muiesan ML, Montani G, Zulli R, Calebich S, Agabiti- Rosei E. Relationship between initial cardiovascular structural changes and daytime and nighttime blood pressure monitoring. Am J Hypertens. 1992;5:180–186.
13. Schmieder RE, Rockstroh JK, Aepfelbacher F, Schulze B, Messerli FH. Gender-specific cardiovascular adaptation due to circadian blood pressure variations in essential hypertension. Am J Hypertens. 1995;8:1160–1166.
14. Framme J, Dangardt F, Mĺrild S, Osika W, Währborg P, Friberg P. 24-h Systolic blood pressure and heart rate recordings in lean and obese adolescents. Clin Physiol Func Imag 2006; 26: 235–239.
15. Cuspidi C, Meani S, Salerno M, Valerio C, Fusi V, Severgnini B, Lonati L, Magrini F, Zanchetti A. Cardiovascular target organ damage in essential hypertensives with or without reproducible nocturnal fall in blood pressure. J Hypertens 2004; 22:273–280
16. Hermida RC, Ayala DE, Mojo´n A, Ferna´ndez JR. (2013e). Blunted sleep-time relative blood pressure decline increases cardiovascular risk independent of blood pressure level – The "normotensive non-dipper" paradox. Chronobiol Int. 30:87–98.
17. An HR, Park S, Yoo T-H, Kang S-W, Ryu J-H, Lee YK, Yang SW, Shin CH. Non-dipper status and left ventricular hypertrophy as predictors of incident chronic kidney disease. J Korean Med Sci 2011; 26:1185–1190
18. Sturrock N, George E, Pound N, Stevenson J, Peck G, Sowter H. Non* dipping circadian blood pressure and renal impairment are associated with increased mortality in diabetes mellitus. Diabetic Med 2000; 17:360–364.
19. Lurbe E, Redon J, Kesani A, Pascual JM, Tacons J, Alvarez V, Batlle D. Increase in nocturnal blood pressure and progression to microalbuminuria in type 1 diabetes. N Engl J Med. 2002;347:797–805. doi: 10.1056/NEJMoa013410.
20. Karavanaki K, Kazianis G, Konstantopoulos I, Tsouvalas E, Karayianni C. Early signs of left ventricular dysfunction in adolescents with type 1 diabetes mellitus: the importance of impaired circadian modulation of blood pressure and heart rate. J Endocrinol Invest 2008; 31: 289–296.
21. Mitsnefes MM, Kimball TR, Daniels SR. Office and ambulatory blood pressure elevation in children with chronic renal failure. Pediatr Nephrol 2003; 18:145–149
22. Ermis N, Otlu YO, Afsin A, Hidayet S, Acikgoz N, Cansel M, et al. Comparison of left atrial volume and function in non-dipper versus dipper hypertensives: A real-time three-dimensional echocardiography study. Anatolian journal of cardiology. 2016;16(6):428-33.
23. Macumber IR WN, Halbach SM, Hanevold CD, Flynn JT. The Association of Pediatric Obesity With Nocturnal Non-Dipping on 24-Hour Ambulatory Blood Pressure Monitoring. American Journal of Hypertension. 2016;29(5):647-652.
24. Redfield MM JS, Burnett JC Jr, Mahoney DW, Bailey KR, Rodeheffer RJ. Burden of systolic and diastolic ventricular dysfunction in the community: appreciating the scope of the heart failure epidemic. JAMA. 2003 Jan 8;289(2):194-202.