www.nephropathol.com DOI: 10.34172/jnp.2022.06 J Nephropathol. 2022;11(1):e06

Journal of Nephropathology

Blood pressure variability in diabetic patients with or without albuminuria

Zahra Davoudi, Majid Salmanian Mashhadi, Navid Mokhtari, Mehdi Sheibani*

Clinical Research Development Center, Loghman Hakim Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran

ARTICLE INFO

Article type:
Original Article

Article history:
Received: 10 July 2020
Accepted: 7 October 2020
Published online: 30 October 2020

Keywords:
Diabetes
Microalbuminuria
Blood pressure
Dipper and non-dipper pattern

ABSTRACT

Introduction: Various studies considered albuminuria as one of the first asymptomatic paraclinical manifestation of the micro-vascular damages in type 2 diabetes mellitus (DM). Hypertension (HTN) is common in type 2 DM, which has a correlation with the greater risks of cardiovascular morbidity and death.

Objectives: The present research evaluated the relationship between blood pressure (BP) variability in diabetic patients who have or not albuminuria.

Patients and Methods: In this analytical-descriptive research, we divided 90 type 2 diabetic patients into two groups of micro-albuminuric (urinary albumin excretion ≥30 mg/d and <300 mg/d) and the normo-albuminuric (urinary albumin excretion <30 mg/d) diabetic patients. We evaluated systolic and diastolic BP and 24-hour Holter monitor BP and heart rate, with respect to their albuminuric states and glomerular filtration rate (GFR) stages.

Results: According to the findings, a considerably greater BMI (body mass index) and retinopathy was observed in microalbuminuric group in comparison with the normoalbuminuric group (P<0.05). Additionally, non-dipping pattern was greater in the microalbuminuric patients (P<0.05). In addition, patients were divided into dippers and non-dippers, the mean daytime and nighttime BP and heart rate were compared. Mean arterial BP (MAP) and nighttime BP and substantially in the subgroup of patients with GFR below 60 mL/min, systolic blood pressure (SBP) were considerably greater in the micro-albuminuric patients (P<0.05).

Conclusion: In patients with diabetes, the existence of albuminuria is related to the increase in the incidence of non-dipping pattern compared with patients without albuminuria. According to high levels of SBP in albuminuric patients with low GFR, the pattern of HTN and then albuminuria and the subsequent reduction of renal function can be similar to that of type 1 DM patients. Moreover, 24-hour Holter monitoring and BP should be monitored closely in diabetic patients.

Implication for health policy/practice/research/medical education:
In this cross-sectional study on 90 diabetic patients, we found albuminuria is associated with non-dipper pattern of blood pressure compared with patients without albuminuria.

Please cite this paper as: Davoudi Z, Salmanian Mashhadi M, Mokhtari N, Sheibani M. Blood pressure variability in diabetic patients with or without albuminuria. J Nephropathol. 2022;11(1):e06. DOI: 10.34172/jnp.2022.06.

Introduction

Hypertension (HTN) has been introduced as one of the key risk factors, both for the coronary artery disease and microvascular complications of diabetes (1). One of the early asymptomatic manifestations of the micro-vascular damages in diabetes is albuminuria which can lead to malfunction of glomerular filtration barriers (2).

Between patients with diabetes, the presence of kidney damage markedly increases cardiovascular risk and health care costs (3). It has recently been indicated that changes in the blood pressure (BP) as well as the average BP possibly correlated with cardiovascular risks (4).

Studies in type 1 diabetic patients have shown that high SBP may occur earlier than microalbuminuria and suggested that nocturnal HTN may have a role in predicting individuals at risk for renal dysfunction (5).

*Corresponding author: Mehdi Sheibani, Email; m.sheibani@sbmu.ac.ir

Original Article

Objectives

In this study, we aimed to study the association between BP variability and albuminuria in diabetic patients.

Patients and Methods

Study design

We conducted a cross-sectional descriptive study on 90 type 2 diabetic patients referred to the endocrine clinic of Loghman-Hakim hospital. Forty-five patients in group A with microalbuminuria (urinary albumin excretion ≥30 mg/d and <300 mg/d) and 45 patients in group B without albuminuria (urinary albumin excretion <30 mg/d) were evaluated. The exclusion criteria were acute infections, inflammations, advanced heart, renal, and liver failure, and malignancy. We gathered data of the BMI (body mass index; kg/m^2), age, diabetes duration, history of the chronic diabetes complication (macrovascular, microvascular), and gender. Then, blood samples of all participants were collected and then we measured hemoglobin A1c (HbA1c), low-density lipoprotein cholesterol (LDL-C), fasting blood sugar (FBS), triglyceride, creatinine, high-density lipoprotein (HDL-C), and total cholesterol. In addition, we used turbidometric test on 24-hour urine collection to determine concentration of the urinary albumin. Moreover, we utilized Cockroft-Gault formula to calculate glomerular filtration rate (GFR mL/min).

Additionally, BP was assessed after ten minutes in the resting position. Accordingly, 24-hour Holter monitoring of BP and heart rate (HR) was also used in all patients to evaluate mean arterial BP (MAP), daytime BP, nighttime BP and nocturnal BP decrease (dipping). Patients were defined as dippers when nighttime systolic BP (SBP) and diastolic BP (DBP) fell more than 10% (normal pattern) and as nondippers when nighttime BP fell less than 10% (abnormal pattern). In both groups, daytime and nighttime and nocturnal BP patterns and the SBP and DBP were compared.

Statistical analysis

For qualitative and quantitative variables, we utilized independent t-test, chi-square and Fisher's exact test for comparing both groups. Also the, level of significance has been considered < 0.05. The data were analyzed by SPSS program (version 24.0) analyzed.

Results

Patients were classified into two groups; microalbuminuria (45 patients; group A) and normoalbuminuria (45 patients; group B). Table 1 displays patients' biochemical and demographic features.

Results did not show any significant differences between the groups in terms of their gender, age, diabetes duration, complications of diabetes, SBP, DBP, LDL-C, HbA1c, cholesterol, HDL-C, and triglyceride levels. BMI and retinopathy in microalbuminuric group were significantly greater than that of normoalbuminuric group ($P<0.05$).

Number of the non-dippers has been considerably greater in the microalbuminuric group (66%) than the normoalbuminuric group (48%) ($P<0.05$; Figure 1).

Groups A and B were compared separately in terms of dippers and non-dippers. In dippers, night time BP significantly was low in group B ($P<0.05$). In non-dippers, MAP and nighttime BP considerably were low ($P<0.05$, Table 2).

The participants also divided into two sub-groups of GFR <60 mL/min or GFR ≥ 60 mL/min, and the mean daytime and nighttime BP as well as the heart rate were compared in these subgroups (Table 3). In both groups, daytime and nighttime BP was lower in group B, however it has been not significant statistically. In subgroup of the participants who had GFR below 60 mL/min, SBP has been greater in group A compared to group B ($P<0.05$).

Discussion

The present study indicates that diabetic patients with

Table 1. Basic characteristics of participants

Variables		Group A	Group B	*P* value
Gender	Men	20 (44%)	21 (46%)	0.59
	Women	25 (56%)	24 (54%)	
Age (year)		62.18±20.2	57.76±7.8	0.30
BMI (kg/m^2)		29.89±5.4	25.99±3.9	0.004*
Diabetes Duration		11.18±6.14	9.37±3.8	0.18
Systolic BP		124.84±11.6	120.88±17.4	0.32
Diastolic BP		76.67±4.9	74.62±8.7	0.28
FBS (mg/dL)		135.46±38.0.	132.64±60.0	0.79
HbA1c (%)		7.76±1.1	8.20±3.1	0.38
Creatinine (mg/dL)		1.15±0.5	1.06±0.3	032.
HDL-C (mg/dL)		46.42±10.4	42.95±12.7	0.17
LDL-C (mg/dL)		88.51±33.18	89.04±28.05	0.93
TG (mg/dL)		160.93±71.6	146.66±65.3	0.32
Cholesterol (mg/dL)		158.18±61.8	147.80±69.1	0.45
GFR (mL/min)		74.53±24.2	76.33±25.5	0.73
CVA	+	1	2	0.50
	-	44	43	
Retinopathy	+	44	9	0.00*
	-	1	36	
Neuropathy	+	33	35	0.30
	-	12	10	
CVD	+	2	1	0.30
	-	43	44	

BMI, body mass index; FBS, fasting blood sugar; LDL, low-density lipoprotein; HDL, high-density lipoprotein; GFR, glomerular filtration rate; TG, triglycerides; CVA, cerebrovascular accident; CVD, cardiovascular disease.

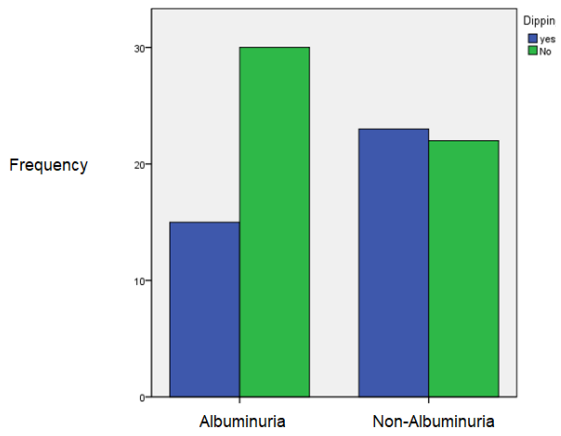

Figure 1. The frequency of the dipper and non-dipper pattern in group A (albuminuria) and B (normoalbuminuria).

albuminuria had a loss of nocturnal BP decline. In fact, albuminuria has been introduced as one of the earliest manifestations of the micro-vascular injuries in diabetes, which is characterized by the onset or progression of diabetic nephropathy (5).

This research revealed greater BMI in the albuminuric patients in comparison with the normo-albuminuric participants, reflecting contribution of overweight and obesity to development of the kidney injury (6,7). In albuminuric patients, retinopathy was found to be higher compared to the normoalbuminuric ones, which confirmed this finding with retinopathy and chronic kidney disease in type 2 diabetes, and is compatible with the study by Kumar et al (8).

We also observed greater nondipping pattern in albuminuric group in BP Holter monitoring. Although in this study, the mean of SBP or DBP and daytime BP showed no difference in both groups, nighttime BP considerably increased in albuminuric group in both dippers and nondippers.

In studies by Okada et al and Torffvit et al, in diabetic patients, the significant relationship of the night time SBP with albuminuria was observed (9,10).

Albuminuria itself is a marker of chronic kidney disease since numerous investigations reflected the increased prevalence of nondippers in chronic kidney disease (11,12). However, few studies have evaluated the

Table 2. Blood pressure and heart rate parameters in groups in two groups of dippers and non-dippers

Variables	Dippers			Non-dippers		
	Group A (n=15) (Mean ± SD)	Group B (n=23) (Mean ± SD)	*P* value	Group A (n=30) (Mean ± SD)	Group B (n=22) (Mean ± SD)	*P* value
MAP overall	98.40±11.2	91.8±11.5	0.97	98.26±12.3	90.30±10.2	0.04*
Day-time BP	101.20±10.9	94.43±10.8	0.69	99.76±12.6	94.22±10.7	0.94
Night-time BP	88.46±11.3	83.17±13.4	0.04*	96.43±12.9	92.4±11.6	0.01*
Systolic BP	130.00±6.7	131.05±20.5	0.88	130.50±16.2	130.15±21.2	0.89
Diastolic BP	77.28±5.8	81.31±22.4	0.25	79.82±8.2	89.28±24.7	0.29
Overall HR	68.66±9.5	72.5±8.7	0.41	71.06±8.5	69.3±8.2	0.21
Day-time HR	71.5±9.1	75.39±9.1	0.39	73.9±8.6	71.86±8.8	0.19
Night-time HR	64.8±8.8	65.8±9.8	0.60	66.30±8.1	64.3±8.1	0.56

BP: blood pressure; HR: heart rate; MAP: mean arterial pressure

Table 3. Blood pressure and heart rate parameters according to GFR in groups A and B

Variables	GFR≥60 (mL/min)			GFR <60 (mL/min)		
	Group A (n=37) (Mean ± SD)	Group B (n=38) (Mean ± SD)	*P* value	Group A (n=8) (Mean ± SD)	Group B (n=7) (Mean ± SD)	*P* value
MAP overall	97.20±11.1	93.3±10.6	0.13	101.62±16.0	88.42±12.05	90.0
Day-time BP	99.48±11.3	95.05±10.4	0.08	103.25±16.4	90.42±12.1	0.10
Night-time BP	91.82±11.8	88.44±13.1	0.25	99.12±15.5	83.7±14.2	0.06
Systolic BP	79.45±7.9	81.17±11.0	0.46	78.12±6.5	110.0±52.1	0.10
Diastolic BP	130.88±14.8	136.11±13.9	0.13	128.12±11.3	93.0±20.4	0.01*
Overall HR	70.97±8.9	70.86±8.6	0.96	69.75±8.7	68.71±8.5	0.66
Day-time HR	74.17±8.7	73.3±9.1	0.68	71.75±7.9	75.5±9.2	0.41
Night-time HR	66.4±8.3	65.05±9.26	0.48	64.7±9.0	65.42±8.1	0.88

BP: blood pressure; HR: heart rate; MAP: mean arterial pressure
*Independent t-test.

association of albuminuria and nocturnal HTN. O'Flynn et al conducted a systematic review and did not find a conclusive association between the isolated nocturnal HTN and the targeted organ damages in diabetes mellitus (13). Gavira et al confirmed the association of elevated nocturnal BP with development of microalbuminuria (14).

Some reports showed significant changes in circadian heart rate in diabetic patients and patients with chronic kidney disease. Knudsen et al showed the impaired nocturnal BP decrease, smoking, and ambulatory BP are robust independent predictors of the development of nephropathy in the patients with type 2 diabetes (15). However, we observed no differences between daytime and nighttime heart rate in the two groups of albuminuria and no albuminuria.

Patients were classified according to GFR, as ≥60 and <60 mL/min since high SBP has been prominent in albuminuric patients with lower GFR.

These findings explained the early pathogenesis of HTN and renal impairment in diabetic patients. These findings are in line with other studies (9,16).

Increased extracellular volume and the predominance of sympathetic activity are thought to be the mechanisms of non-dipping pattern in diabetes (17), while non-dipping was closely associated with autonomic neuropathy and renal injury and proteinuria too (7,15,18).

We excluded higher stages of chronic kidney disease (GFR <30 mL/min) in this study. We think that if we had patients with higher stages of renal failure, we could find more significant differences in BP Holter monitoring in the two groups of chronic kidney disease patients.

Conclusion

Based on results, in diabetic patients who had similar demographic and laboratory characteristics, the existence of albuminuria had an association with the increase in the occurrence of non-dipping patterns compared to patients without albuminuria. Given the high levels of SBP in albuminuric patients with low-GFR, the pattern of HTN, albuminuria, and the subsequent reduction of renal function can be similar to that of patients with type 1 diabetes.

Limitations of the study

Notably, patients with DM with or without HTN, as well as the patients who did not have adequate BP control, did not receive a separate assessment. Because of the limited sample size, the distribution of patients with albuminuria to the two groups of micro- and macroalbuminuria and the comparison of these two groups was not possible. It is recommended that more studies be conducted and that a 24-hour BP Holter should be performed at least once to assess the nighttime BP and the non-dipper BP pattern in patients with diabetes.

Acknowledgments

The Clinical Research Development Center of Loghman Hakim Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran is highly appreciated.

Authors' contribution

ZD, MSM, NM, and MSH conducted the research. ZD and MSM assisted in the preparation of this paper. ZD and MSH procured the resulting paper. The resulting paper has been read by each author and then signed.

Conflicts of interest

It is declared that there are not any conflicts of interest.

Ethical issues

The Declaration of Helsinki and the pertinent instructions of the ethics committee of the Ministry of Health have been followed in each stage of the study. Moreover, each participant has been asked to sign the informed consent forms. In addition, the ethics committee of Shahid Beheshti University of Medical Sciences approved the study (#IR.SBMU.MSP.REC.1396.523). The present research has been extracted from the internal medicine residential thesis of Majid Salmanian Mashhadi. Moreover, ethical issues including plagiarism, double publication, and redundancy have been completely observed by the authors.

Funding/Support

The present research has been funded by Shahid Beheshti University of Medical Sciences. It has been extracted from the residency thesis of Majid Salmanian Mashhadi.

References

1. de Boer IH, Bangalore S, Benetos A, Davis AM, Michos ED, Muntner P, et al. Diabetes and hypertension: a position statement by the American Diabetes Association. Diabetes Care. 2017;40(9):1273-84. doi: 10.2337/dci17-0026.
2. Hellemons ME, Kerschbaum J, Bakker SJ, Neuwirt H, Mayer B, Mayer G, et al. Validity of biomarkers predicting onset or progression of nephropathy in patients with Type 2 diabetes: a systematic review. Diabet Med. 2012;29(5):567-77. doi: 10.1111/j.1464-5491.2011.03437.x.
3. Fox CS, Matsushita K, Woodward M, Bilo HJ, Chalmers J, Heerspink HJ, et al. Associations of kidney disease measures with mortality and end-stage renal disease in individuals with and without diabetes: a meta-analysis. Lancet. 2012;380(9854):1662-73. doi: 10.1016/S0140-6736(12)61350-6.
4. Rothwell PM, Howard SC, Dolan E, O'Brien E, Dobson JE, Dahlof B, et al. Prognostic significance of visit-to-visit

variability, maximum systolic blood pressure, and episodic hypertension. Lancet. 2010;375(9718):895-905 doi: 10.1016/S0140-6736(10)60308-X.
5. Ninomiya T, Perkovic V, de Galan BE, Zoungas S, Pillai A, Jardine M, et al. Albuminuria and kidney function independently predict cardiovascular and renal outcomes in diabetes. J Am Soc Nephrol. 2009;20(8):1813-21. doi: 10.1681/ASN.2008121270.
6. Rathore JA, Abid D, Saleem M. Microalbuminuria in diabetes mellitus type 2: Association with age, sex, and body mass index: A Cross sectional study. Med Forum. 2015;26:21-3.
7. Ruiz-Hurtado G, Ruilope LM, de la Sierra A, Sarafidis P, de la Cruz JJ, Gorostidi M, et al. Association between high and very high albuminuria and nighttime blood pressure: influence of diabetes and chronic kidney disease. Diabetes Care. 2016;39(10):1729-37. doi: 10.2337/dc16-0748.
8. Verma AK, Sinha RK, Saxena N, editors. Association of Pulse Pressure and Diurnal Blood Pressure Variation with Micro- and Macrovascular Complications in Type 2 Diabetes in Rohilkhand Region. International Journal of Contemporary Medical Research. 2018.
9. Torffvit O, Tapia J, Rippe B, Alm P, Willner J, Tencer J. Ambulatory blood pressure in type 2 diabetic patients with albuminuria: relation to the renal function and structural lesions. J Diabetes Complications. 2004;18(6):328-35. doi: 10.1016/j.jdiacomp.2004.03.004
10. Okada H, Fukui M, Tanaka M, Inada S, Mineoka Y, Nakanishi N, et al. Visit-to-visit variability in systolic blood pressure is correlated with diabetic nephropathy and atherosclerosis in patients with type 2 diabetes. Atherosclerosis. 2012;220(1):155-9. doi:10.1016/j.atherosclerosis.2011.10.033
11. Duggal A, Bal B, Singh N. Study of dipping and non-dipping patterns in patients of type 2 diabetes mellitus with hypertension and its association with microalbuminuria. Ann Int Med Den Res. 2017;3:20-24. doi: 10.21276/aimdr.2017.3.2.ME6
12. Hogan D, Lurbe E, Salabat MR, Redon J, Batlle D. Circadian changes in blood pressure and their relationships to the development of microalbuminuria in type 1 diabetic patients. Curr Diab Rep. 2002;2(6):539-44. doi: 10.1007/s11892-002-0125-z
13. O'Flynn AM, Madden JM, Russell AJ, Curtin RJ, Kearney PM. Isolated nocturnal hypertension and subclinical target organ damage: a systematic review of the literature. Hypertens Res. 2015;38(8):570-5. doi: 10.1038/hr.2015.43.
14. Mateo-Gavira I, Vilchez-Lopez FJ, Garcia-Palacios MV, Carral-San Laureano F, Jimenez-Carmona S, Aguilar-Diosdado M. Nocturnal blood pressure is associated with the progression of microvascular complications and hypertension in patients with type 1 diabetes mellitus. J Diabetes Complications. 2016;30(7):1326-32. doi: 10.1016/j.jdiacomp.2016.05.021.
15. Knudsen ST, Laugesen E, Hansen KW, Bek T, Mogensen CE, Poulsen PL. Ambulatory pulse pressure, decreased nocturnal blood pressure reduction and progression of nephropathy in type 2 diabetic patients. Diabetologia. 2009;52(4):698-704. Doi: 10.1007/s00125-009-1262-6
16. Okada H, Fukui M, Tanaka M, Matsumoto S, Mineoka Y, Nakanishi N, et al. Visit-to-visit blood pressure variability is a novel risk factor for the development and progression of diabetic nephropathy in patients with type 2 diabetes. Diabetes Care. 2013;36(7):1908-12. doi: 10.2337/dc12-2087
17. Pecis M, Azevedo MJ, Moraes RS, Ferlin EL, Gross JL. Autonomic dysfunction and urinary albumin excretion rate are associated with an abnormal blood pressure pattern in normotensive normoalbuminuric type 1 diabetic patients. Diabetes Care. 2000;23(7):989-93. doi: 10.2337/diacare.23.7.989.
18. Oh SW, Han SY, Han KH, Cha R-h, Kim S, Yoon SA, et al. Morning hypertension and night non-dipping in patients with diabetes and chronic kidney disease. Hypertens Res. 2015;38(12):889-94. doi: 10.1038/hr.2015.89.