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COMPARISON OF THE AMBULATORY BLOOD PRESSURE VARIABILITY IN DIABETIC HYPERTENSIVE AND NON DIABETIC HYPERTENSIVE PATIENTS

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Contribution

NA conceived the idea and designed and wrote the study. MM and KAH helped in data collection and analysis. MTMUD, MAK did final review. All authors contributed equally to the submitted manuscript.

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ABSTRACT

Objective: To examine the possible difference in the short-term BP variability between diabetic and non-diabetic hypertensives.

Methodology: It is a prospective observational cohort study. The present research was carried out in cardiology ward of Bahawalpur Victoria Hospital for the duration of six months from 01-06-2018 to 30-11-2018. 392 patients between 18 years to 60 years of age, including both genders are recruited in the study who are diabetic-hypertensives (exposed group) and hypertensives without diabetes ((unexposed group) and blood pressure <140/90 mmHg by drugs

Results: We measured 24-hr ambulatory BP in 196 diabetic hypertensive (diabetic HTN) and 196 non-diabetic hypertensive (non-diabetic HTN). There were no statistically significant differences in ambulatory day time systolic BP (130.71 mmHg vs. 128.88 mmHg), and night time ambulatory systolic BP (129.03 mmHg vs. 136.68 mmHg) between diabetic HTN and non-diabetic HTN. Diabetic HTN had a significantly greater day ambulatory systolic and diastolic BP variability than non-diabetic HTN (4.80 mmHg vs. 4.18 mmHg, $p < 0.05$; 3.64 mmHg vs. 2.80 mmHg, $p < 0.05$, respectively) and diabetic HTN had a significantly greater night systolic and diastolic BP variability than non-diabetic HTN (4.99 mmHg vs. 3.88 mmHg, $p < 0.05$; 3.39 mmHg vs. 2.82 mmHg, $p < 0.05$, respectively).

Conclusion: These results demonstrate that BP variability is increased in diabetic hypertensive. It is noted that fasting blood glucose level were found to be raised in patients with increased BP variability.

Key Words: Ambulatory blood pressure, Variability in blood pressure

INTRODUCTION

Diabetes and hypertension are a critical combination for the development of both macro and micro vascular disease. Presently, diabetic patients are rapidly increasing in number and cardiovascular complications are the most common cause of death in patients with diabetes.[1] Thus it would be of considerable value to identify the precise mechanism involved in the cardiovascular events associated with diabetes.

Ambulatory blood pressure monitoring has allowed an easier and more accurate determination of circadian rhythm of blood pressure under different pathophysiological conditions. Ambulatory blood pressure monitoring allows the acquisition of information not only on the average of 24 hour24-hour blood pressure, but also on the variations that characterize the blood pressure values in the course of daily life. Ambulatory blood pressure monitoring has also allowed an easier and more accurate determination of the circadian rhythm of the blood pressure under different pathological conditions, and has enabled to evaluate the effects of antihypertensive drugs. Type 2 diabetic patients often have a deregulation of the autonomic control of cardiovascular function, which is bound to increase blood pressure variability.[2]

In a study 30 diabetic hypertensive patients as compared to their 30 non-diabetic hypertensive showed that there is diabetic HTN (exposed) had a significantly greater 24-hr systolic and diastolic BP variability than non-diabetic HTN (unexposed). The mean of 24 hours systolic ambulatory BP is 125 with standard deviation 31.75 in diabetic HTN (exposed) while mean of 24hours systolic ambulatory BP is 116.8 with standard deviation 35.13 in non-diabetic HTN(unexposed). Raised fasting blood glucose levels are associated with increased BP variability in diabetic patients.[3]

Another study was had done on ambulatory blood pressure monitoring (ABPM) in 300 patients with uncomplicated type-2 diabetes mellitus (T2DM) without known CVD and without BP medications. It showed that mean age of diabetic was 67.8 ± 9.6 years, 48% were male, 253 (84%) had a diagnosis of hypertension. The mean of the standard deviations of awake ambulatory systolic BP (T2DM and hypertensive) was 18 ± 6 and ambulatory diastolic BP (T2DM and hypertensive) was 11 ± 4 mm Hg. Those of sleep the mean of the standard deviations of ambulatory sleep systolic BP(T2DM and hypertensive) was 13 ± 5 and ambulatory diastolic BP (T2DM and hypertensive) was 9 ± 3 mm Hg. During follow-up, there were 29 cardiovascular events. In this multivariable analysis, the standard deviations of ambulatory sleep Systolic BP (T2DM and hypertensive) was independently associated with incident Coronary vascular disorders (CVD). Neither the non-dipper and riser patterns nor the morning BP (T2DM and hypertensive) surge were associated with incident CVD events independently of clinic and 24-hours BP levels.[6]

In anotherA study among on 7,458 subjects randomly recruited from six populations,5those with higher night time than daytime blood pressure had a higher risk of death. However, reverse dippers were more frequently on anti hypertensive drug treatment, were also older, and more often had a history of diabetes mellitus or previous cardiovascular disease.[5]

The rationale of this study is to examine the mean blood pressure variability in hypertensive subjects with or without diabetes. If variability is detected, then further studies could be undertaken to assess the association of mean ambulatory blood pressure variability and cardiovascular risk.

METHODOLOGY

It is a prospective observational cohort study. The study was conducted in cardiology ward of Bahawalpur Victoria Hospital for the duration of six months from 01-06-2018 to 30-11-2018. 392 patients between between 18 years to 60 years of both genders are included in study who are diabetic-hypertensive (exposed) and hypertensives without diabetes ((unexposed) and blood pressure optimally (<140/90 mmHg) controlled by antihypertensive pharmacological treatment in both groups (diabetic and non-diabetic).The following subjects were excluded from the study:

1. Patients known to have secondary hypertension or chronic renal failure ((Serum creatinine >2mg / dl) confirmed clinical history)).

2. Patients with type1 diabetes, type2 diabetics with serious comorbidity like diabetic neuropathy, diabetic foot, diabetic retinopathy, diabetic nephropathy requiring hospitalization (on history)

3. Gestational diabetics (on history)

Sample size was calculated by using statistics, 16.83 ± 8.45, 14.6 ± 7.3 and 1-β=80%, 196 samples had included in each group.3(196 diabetic hypertensive and 196 non-diabetic hypertensive) via non probability consecutive sampling.

After written informed consent, patients were enrolled in study from cardiology ward of Victoria Hospital Bahawalpur and subjected to focused history and physical examination. Their demographic details were also recorded. After explaining the nature of study and procedure, and having informed consent, instructions were being given in full detail. Before taking clinic BP measurement, patients were asked to relax in a quiet room for 15 minutes. Then blood pressure was measured in both the arms. The arm with higher reading was being selected if BP in this arm is ≥10 mmHg more than the other arm, while the non-dominant side was being selected if the difference is <10 mmHg. The oscillometric ambulatory blood pressure device (Tonoport V/2 CE 0482, Ref. 2001589- 038) was applied to the subject for the duration of 24 hours. Waking hours timing was 6 am to 10 pm while sleeping hours timing was 10 pm to 6 am. The device was adjusted to take readings every 30 minutes during waking hours and hourly during sleeping hours. Results on the next day were recorded on a pre-designed proforma.

The data was entered and analyzed by SPSS version 18.0. Gender, diabetic-hypertensive (exposed), non-diabetic hypertensive patients (unexposed) were taken as qualitative variables of the study, which was presented as frequencies and percentages. Age, duration of diabetes, duration of HTN and ambulatory blood pressure (diabetic and non- diabetic patients) were been quantitative variables of the study and will be presented as mean ± standard deviation. The difference between exposed and unexposed groups was measured through independent t test. P value ≤0.05 was been value taken significant. Stratification will be done according to gender, age, duration of diabetes, duration

of hypertension and obesity to control modifiers/confounders applying t test.

RESULTS

A total of 392 patients were included and divided into two groups with 196 in each. Results showed no statistically significant differences in BP values in different patient groups in different BP values including systolic and diastolic values. However, hypertensives with diabetes (called exposed) had significantly greater 24-hr systolic BP variability than the hypertensives without diabetes (unexposed) (5.61 mmHg vs. 4.97mmHg, p =0.00). There were no significant difference in daytime average and night average BP variability in both cases. Comparison among different groups during day and night time shown in tables 1-3

Table 1: Comparison of 24-hr Systolic Blood Pressure Between the Non-Diabetic Hypertensive Group (non-dm) And Diabetic Hypertensive Group (DM)

	DM-HTN		HTN		df	t-value
	Mean	SD	Mean	SD		
24-hr-systolic BP(mmHg)	132.78	5.61	129.87	4.96	390	-7.68
24-hr-diastolic BP(mmHg)	88.15	2.81	86.52	3.57		

Abbreviations: BP = blood pressure, NS = not significant.

Table 2: Comparison of Day Time Systolic and Diastolic Pressure between the Non-diabetic Hypertensive Group (non-dm) and Diabetic Hypertensive Group (DM)

	DM-HTN		HTN		df	t-value
	Mean	SD	Mean	SD		
Day systolic BP (mmHg)	130.71	4.80	128.88	4.18	390	0.00
Day time diastolic (mmHg)	85.92	3.64	88.19	2.80		

Abbreviations: BP = blood pressure, NS = not significant.

Table 3: Comparison of Night Time Systolic and Diastolic Blood Pressure between the Non-diabetic Hypertensive Group (non-dm) and Diabetic Hypertensive Group (DM).

	DM-HTN		HTN		df	t-value
	Mean	SD	Mean	SD		
Night time systolic BP (mmHg)	136.68	3.89	129.03	4.99	390	-16.93
Night time diastolic systolic BP (mmHg)	88.11	2.82	87.12	3.40		

Abbreviations: BP = blood pressure, NS = not significant.

DISCUSSION

Autonomic nervous system (ANS) is the main underlying neurohormonal system controlling BP and its time to time variations in daily life activities. It has also been noted that arterial wall stiffness due to atherosclerotic process also takes part to some extent in controlling these variations. These variations are increased by decrease activity of baro recepters and reduced response of larger elastic arteries in their relaxation when needed due to calcification in walls. Due to these associations, BP variations has also been seen as possible underlying mechanism for development of atherosclerosis and its related prognosis and also progression of this disease. Many past studies has shown in diabetics with macrovascular complications, the trend of BP fall at night is reduced and it is due to dysfunction of ANS. In this study, we focused on BP variability and different factors in hypertensives with diabete.7

About 30 diabetic hypertensive patients as compared to their 30 non-diabetic hypertensive showed that hypertensives with

diabetes (called exposed) had a significantly higher systolic and diastolic BP variations in the whole day than hypertensives without diabetes (called unexposed). The mean of 24 hours systolic ambulatory BP is 125 with standard deviation 31.75 in exposed group while mean of 24hours systolic ambulatory BP is 116.8 with standard deviation 35.13 in unexposed group. High fasting blood glucose is associated with increased BP variability in diabetic patients .3 These results are consistent with our study.

Another study had done on ambulatory blood pressure monitoring (ABPM) in 300 patients with uncomplicated type-2 diabetes mellitus (T2DM) without known CVD and without BP medications. The mean of the standard deviations of awake ambulatory systolic BP (T2DM and hypertensive) was 18 ± 6 and ambulatory diastolic BP (T2DM and hypertensive) was 11 ± 4 mm Hg. During sleep the mean of the standard deviations of ambulatory systolic BP(T2DM and hypertensive) was 13 ± 5 and ambulatory diastolic BP (T2DM and hypertensive) was 9 ± 3 mm Hg. During follow-up, there were 29 cardiovascular events. CAD is also independently more prevalent during day as well as during night in patients who have more blood pressure variability 6

In another study among 7,458 subjects randomly recruited from six populations,5 those with higher night time than daytime blood pressure had a higher risk of death. These reverse dippers were more frequently on antihypertensive drug treatment, were also older, and more often had a history of diabetes mellitus or previous cardiovascular disease.[5]

Our study showed that BP control was same in both hypertensives with and without diabetes (exposed and unexposed) during day time. During night BP fall was also same in our both study groups. However, importantly, 24-hr BP variations were significantly greater in the hypertensives with diabetes (exposed group). [4]

Multiple reasons may be responsible for the increase in BP variations in the exposed group. It is possible that renal functional state is related to BP variability in connection with volume state and neuroendocrine systems. DM+HTN patients had a significantly higher nighttime systolic BP than patients with non-DN in spite of similar daytime BP levels.[8]

Our study showed that FBS level has strong association with BP variations over 24 hours. So in diabetics hypertensive, it is high blood sugar responsible for variations in BP control. In the past, the Ohasama done a research that showed various other factors like age, pulse pressure, and BMI were also related to BP variations. Several other researches also depict BP variations to be governed by ANS balance and arterial compliance. Thus BP variations are possibly controlled by blood sugar directly or indirectly controlled by the activation of sympathetic nervous system induced by high blood glucose.

Importantly, high blood glucose results in the activation of local neuro-hormonal system, increasing the progression of arterial wall stiffness. Thus, there could be much less arterial wall compliance in diabetic hypertensive than in non-diabetic hypertensives.[9]

Diabetics has increased wall stiffness and decrease arterial compliance in ARIC study. Other researches has shown in elderly ankle brachial index is related to blood sugar level. Results of our study guide that diabetic with hypertension need not only BP control but also strict control of the fasting blood glucose level to efficiently achieve decrease in BP variability.

LIMITATIONS

Limitations of the present study include the small patient number, being under antihypertensive medication, and the lack cardiovascular reflex tests to link the increased BP variability with autonomic neuropathy.10 Further study on BP variability in diabetic hypertensive without nephropathy and normotensive patients with diabetes mellitus, as well as on the mechanism between fasting blood glucose and BP variability,will be needed to clarify these

Limitations of the present study include the small patient number, the cross-sectional analysis, being under antihypertensive medication, and the lack cardiovascular reflex tests to link the increased BP variability with autonomic neuropathy.[10] Further study on BP variability in diabetic hypertensive without nephropathy and normotensive patients with diabetes mellitus, as well as on the mechanism between fasting blood glucose and BP variability, will be needed to clarify these important issues.

CONCLUSION

Blood pressure variability is increased in diabetic hypertensive patients as compare to non- diabetic hypertensive patients

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