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Research International Journal of Endocrinology and Diabetes

Research Article

Significance of Measuring Central Systolic Blood Pressure in Type 2 Diabetic Patients: An Observational Study

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Received: 17 July, 2021

Accepted: 28 July, 2021

Published: 29 July, 2021

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Keywords: COVID 19 (Coronavirus disease of 2019), CSBP (Central Systolic Blood Pressure), PSBP (Peripheral Systolic Blood Pressure), RAS blockade (Renin-Angiotensin system blockade), Type 2 diabetes mellitus (T2DM).

Abstract

Background: Data clearly shows a higher incidence of COVID 19 and worse outcomes in patients with diabetes and Hypertension (30,31). Patients with T2DM are at a higher risk of developing cardiovascular disease, which is inadequately explained by conventional risk factors. CSBP is known to correlate with more cardiovascular events than standard mercury based PSBP. Diabetic patients are known to have higher CSBP than non-diabetic individuals. There is a paucity of data about CSBP in diabetic patients in India, hence there is a perceived need for more studies in this area.

Design: Analytic (Cross sectional) observational study.

Methods: The study was approved by the 'Institutional Ethics Committee, Care Hospital', Hyderabad, India. We assessed similar groups of T2DM patients and healthy individuals for CSBP measurement by "Pulsecor - BP+" device and compared them with standard mercury based brachial PSBP measurement. In hypertensive diabetic patients, the differences in the effect of various antihypertensive agents on PSBP & CSBP was also studied.

Results: We found that a higher number of participants (T2DM 73% versus 61%, healthy individuals 22% versus 16.6%) had uncontrolled CSBP than the number of patients with high PSBP $p < 0.01$). In addition, it was observed that CSBP was better controlled in patients on RAS blockade drugs than in those receiving beta blockers (33% versus 23%).

Conclusion: This study highlights the importance of measuring CSBP in T2DM patients to identify and treat those who would otherwise be missed by measuring only PSBP.

Introduction

In the light of the ongoing pandemic of COVID 19, it has been evident that diabetes and hypertension have been among the top comorbidities globally. This was reflected in a retrospective analysis of patients with COVID-19, where those with diabetes were seen to have a greater incidence of hypertension (56·9%), cardiovascular disease (20·9%), compared to those without diabetes (28·8%, and 11·1%, respectively). In addition, in the patients with diabetes, it was noted that the deceased had a greater prevalence of comorbidities than those who survived (hypertension 83·9% vs 50·0%) (32). Undoubtedly, hypertension remains a major risk factor for cardiovascular diseases (CVD) and all-cause mortality [1].

Additionally, type 2 Diabetes mellitus (T2DM) poses a significant risk for cardiovascular and renal diseases as well [2]. This is evident from numerous studies which indicate that T2DM is commonly associated with hypertension; and patients with both the comorbidities indeed have greater prevalence of renal and cardiovascular risks than those with either hypertension or diabetes [3, 4]. Hence, optimal evaluation and management of blood pressure (BP) in diabetic patients with hypertension is crucial in preventing complications. There is plenty of evidence to demonstrate that controlling peripheral BP is instrumental for reduction of future cardiovascular and renal events.

However, a lot of data has emerged indicating that traditional brachial artery BP measurement may not necessarily represent central BP which is measured in the aortic artery [5, 6]. Furthermore, many clinical trials signify that patient with high central BP have considerably

higher cardiovascular risk in comparison with those with low central BP, implying central BP as an independent predictor for CVD [7]. Moreover, there are very few studies so far specifically looking at the relevance of central BP in Indian patients with diabetes and hypertension [28, 29]. The aim of our study was to evaluate the control of CSBP versus PSBP in T2DM patients and healthy individuals; and observe and compare the control of CSBP by various antihypertensive groups.

Methods

The study was approved by the 'Institutional Ethics Committee, Care Hospital', Hyderabad, India.

Participants in Study

Type 2 diabetic patients were included from our clinic database after written informed consent while healthy individuals were selected after proper clinical questionnaire and informed consent excluding acutely diseased persons. About 508 type 2 diabetic patients and 510 healthy volunteers with essential hypertension as inclusion criteria were recruited. (Table 1) shows basic characteristics of T2DM patients included in the study. Among 510 healthy individuals, the mean age 32.54+/-10.16 years and mean body mass index was 26.15+/- 6.25 kg/meter^2.

Data Collection

We used structured questionnaires to gather demographic data including age, sex, duration of diabetes and hypertension and current medications. Patient baseline examination data of height, weight and heart rate and peripheral BP at rest was collected by 2 investigators independently. As per WHO definition, we calculated body mass index (BMI) for all the participants by dividing body weight in kilograms by height in square meters.

We used the standard JNC7 guideline recommendation for measurement of peripheral BP [8], which in the patient sitting upright quietly for 10 minutes with the non-dominant arm resting at the heart level. Total 3 BP readings were derived with 1 minute interval between each reading and mean BP was calculated. For **Central BP measurement,** participants were asked to fast for at least 8 hours prior and omit their medications in the morning. We used applanation tonometry with Pulsecor device [9, 10] which involved use of radial pulse and a validated generalized transfer function to extract central BP from the peripheral signal. Prior to measuring CBP, participants were fasting for at least 8 hours and no medications were used the same morning. Participants were put in a supine position for 10 minutes.

Statistical Analysis

The data was classified as categorical and non-categorical variables. The observed frequencies of categorical variables were analyzed using 2 x 2 Chi Square test while mean of the 2 groups were compared by 'Student's' t test.

Results

Among all T2DM patients, 356/508 (70%) were known hypertensive who were already on antihypertensive therapy, while 152 (30%) patients had no history of hypertension. Of these 152 patients, 107 (70%) had high CSBP (> 125 mm of Hg), while 87/152 (57%) had PSBP > 140 mm of Hg (Figure 1), newly detected hypertensive, p<0.001) Mean PSBP & mean CSBP in healthy individuals were (120.6 + 15.29) & (110.17 + 15.96) mm of Hg. Thus, the number of newly detected hypertensive patients in healthy individuals were significantly lower than those in type 2 diabetes group (PSBP > 140 mm of Hg, 87/152 versus 85/510, p < 0.001) (Table 2). Among all T2DM patients,138/508 (27%) had normal central aortic pressure (< 125 mm of Hg) while 199/508 (39%) had normal peripheral systolic pressure (<140 mm of Hg) (P<0.001). Also, more no. of patients in RAS blockade group 95/157 (37.5%) had central systolic blood pressure in normal range compared to patients on beta blockers 14/60 (23.3%) (Table 3).

Utility and Discussion

Since the World Health Organization (WHO) declared the COVID-19 outbreak as a pandemic, it continues to be a matter of international concern. A lot of recent data concludes the fact that higher incidence of COVID 19 and worse outcomes are seen in patients with diabetes and Hypertension [30, 31]. Numerous epidemiological studies reveal that hypertension is a commonly associated comorbidity with T2DM and these

Table 1: Basic Clinical details of Type 2 diabetic patients in the group.

Parameter	Value ± SD
Age	50.72 ± 11.66 years
Body Mass Index (BMI) kg/m2	30.50 ± 12.6
HbA1C	8.03 ± 5.8%
Duration of diabetes	8 ± 4.2 years
Known Hypertensive (n)	356/508 (70%)
No Hypertension (n)	152/508 (30%)

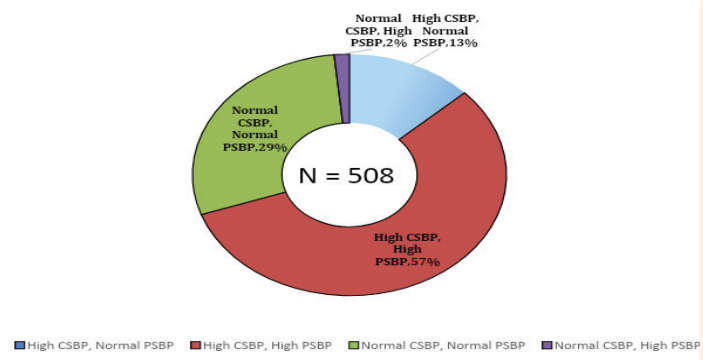

Figure 1: Proportion of Type 2 diabetic patients with 'normal and high' 'central and peripheral systolic pressure'.

Table 2: Newly detected hypertensive patients by CSBP & PSBP measurement among T2DM patients and healthy individuals.

Hypertension criteria (CSBP & PSBP) *	Non hypertensive Type 2 DM (n=152)	Healthy individuals (n=510)
Newly detected hypertensive (CSBP > 125 mm of Hg) #	107/152 (70.4%)	125/510 (22.5%)
Newly detected hypertensive (PSBP > 140 mm of Hg) ##	87/152 (57.2%)	85/510 (16.6%)

*CSBP: Central systolic blood pressure
PSBP: Peripheral systolic blood pressure
# p < 0.01
p < 0.001

Table 3: Proportion of patients under controlled hypertension receiving various antihypertensive agents.

BP	RAS blockade	RAS +	CCB	CCB+	BB	BB+
CSBP ≤ 125	17/75 (22.6%)	79/239 (33%)	6/20 (30%)	52/155 (33%)	9/39 (23%)	51/122 (42%)
PSBP ≤ 140	26/75 (34.6%)	104/239 (43.5%)	6/20 (30%)	65/155 (42%)	15/39 (38%)	45/122 (36.8%)

CSBP: Central Systolic Blood Pressure
PSBP: Peripheral Systolic Blood Pressure
RAS blockade: Renin Angiotensin blockade (+, additional agent)
CCB: Calcium Channel Blockers
BB: Beta blockers

patients tend to have higher renal and cardiovascular risks in comparison with those without hypertension [11]. Therefore, better evaluation and management of BP in diabetic patients with hypertension becomes critically important. The relationship between brachial and central aortic pressure is modified by ageing, disease, and drug therapy. Hence, brachial pressure is not always a perfect surrogate for central aortic pressure.

There is an augmentation in blood pressure as we move from central to peripheral areas. And hence normal brachial systolic blood pressure is considered less than 140 while normal central aortic systolic blood pressure is considered less than 125 mm of Hg [5, 7]. There is a strong argument to believe that cardiovascular events may be linked to central rather than brachial pressure, as major arteries in the body are more reflective of aortic rather than brachial pressure. This theory is backed up by the evidence published over the last decade demonstrating the relationship between central pressure and CV risk [12]. Interestingly, systolic pressure can be variable throughout the course of the arterial tree, in a way that aortic (central) systolic pressure tends to be lower than corresponding brachial values, even though there is considerable interpersonal variation. Hence it is suggested that central pressure correlates better with regards to future risk of cardiovascular events than brachial pressure [5]. There is good evidence from various studies such as the Framingham heart study, to indicate that the pulsatile component of the hemodynamic load of the heart is a better predictor of cardiovascular events than steady component of either systolic or diastolic pressure [14, 19]. There are noninvasive methods to assess CSBP, with 90-95% correlation with catheter based invasive measurement of CSBP, e.g. 'Pulsecor' device which measures calculated CSBP from peripheral pulse wave assessment [9, 10]. The degree of augmentation of the central systolic pressure wave can be recorded non-invasively using applanation tonometry of the brachial artery, a validated transfer function, and pulse wave analysis [15-17].

According to several studies CSBP can be used as an important prognostic risk factor for CV events [18], [28]. As lesser cardiovascular events are seen with lower CSBP levels, it becomes paramount to differentiate patients with similar brachial BP but different CSBP. In the Strong Heart Study [5], Roman et al illustrated a stronger link of CSBP to important cardiovascular risk parameters such as vascular hypertrophy, extent of atherosclerosis, and ultimately future cardiovascular events. These findings were also supported in another post-hoc analysis of clinical trial (the ASCOT) [20], where Williams et al found higher rate CV events in those whose CSBP was suboptimal. This was seen in patients despite reasonable control of their brachial BP, indicating central BP being an independent predictor of clinical outcomes. Thus, measurement of peripheral blood pressure alone, can lead to missing out on a good proportion of patients with underlying high CSBP. Our study shows similar findings with a higher number of T2DM patients with uncontrolled CSBP than with high PSBP.

Interestingly, various anti-hypertensive drugs can exert differential effects on brachial and central pressure. Hence, it becomes paramount to devise treatment decisions guided by central BP rather than brachial pressure [13]. Although there are several studies assessing the differential effect of anti-hypertensive drugs, (20,23) a lot of variation is seen in the methodology of measuring CSBP and duration of antihypertensive medications. Moreover, very few studies looked at and analyzed the differential effect of individual classes of anti-hypertensive medications on BP [23-25]. Nevertheless, individual effects of atenolol with the fixed-dose combination of the ACE inhibitor (perindopril) were compared with the diuretic, indapamide in the REASON trial [26].

The results concluded similar reductions in brachial and central pressure in a subset of patients, however reduction in central pressure with atenolol was noted to be approximately half of that in brachial pressure. Additionally, the CAFE sub-study of the ASCOT trial [27] also subsequently reported that despite similar reduction in brachial pressure, the individuals randomized to atenolol were noted to have a 4.3 mmHg higher central systolic pressure than those given amlodipine. Overall in terms of efficacy, numerous studies have shown ACEI or ARB to be better than diuretic or beta-blocker in reducing central BP [29]. Improvement in endothelial dysfunction and vascular fibrosis related to diabetes could explain a superior response to ACEI or ARB in improving aortic stiffness and reducing central BP [20-22]. Our study indicates that patients on ACEI or ARB agents had better CSBP control than patients on beta blockers, although this was not comparable due to disparity in number of patients in both these groups.

Conclusions

Our study suggests that a higher number of T2DM patients than healthy individuals have uncontrolled CSBP than PSBP. Higher number of T2DM patients had uncontrolled CSBP than the number of patients with high PSBP. CSBP was better controlled in patients on RAS blockade drugs than in those on beta blockers. It highlights the importance of considering measuring CSBP in T2DM patients to identify the patients at higher cardiovascular risk and treat those who would be otherwise missed by measuring PSBP only. It is especially important to pick and treat hypertension in patients with type 2 DM in the current scenario of COVID 19 pandemic.

Limitations

The lack of double-blind randomized sampling and a relatively small sample size of patients could affect generalizability (external validity) of our study results. Although there is a possibility of bias caused by patients on anti-hypertensive drugs, we realize that the comparison of efficacy between different antihypertensive agents results need studies with larger sample size and well-matched groups. Moreover, we did not assess the effect of CSBP on the risk of coronary arterial disease or stroke in our patient groups, nevertheless, this was not the primary intention of our study.

Declarations

Consent to Participate: Informed consent was taken from all the participants in the study.

Consent for Publication: NA

Availability of data and materials: The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing Interests: The authors declare that they have no competing interests.

Funding: Self-funded

Authors' Contributions: KDM and VM analyzed and interpreted the patient data regarding CSBP. GA was a major contributor in drafting the work and substantively revising the manuscript. All authors read and approved the final manuscript.

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