Original Article

Arterial stiffness as a screening tool for cardiovascular risk in health and disease

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Abstract

Background: Cardiovascular diseases (CVD) account for approximately one-third of all deaths worldwide. The incidence of cardiovascular events such as myocardial infraction has been reported to be progressively increasing with age, especially with existing comorbidities such as hypertension, diabetes and obesity. Assessing arterial stiffness indices may serve as a screening tool in identification of population at risk of cardiovascular diseases and assist in implementation of preventive measures and early treatment in this population. **Objectives:** To measure and compare the arterial stiffness indices in healthy adults with diabetes, hypertension and obesity. **Methods:** A total of 184 adults in the age group of 30-50 years were included in the study who were divided into 4 groups: Group I (n = 64) (diabetic), group II (n = 40) (hypertensives), group III (n = 40) (obese) and group IV (n = 40) (control). The arterial stiffness indices were measured by using a certified oscillometric device in all the participants. **Results:** The arterial stiffness indices were assessed by using a certified oscillometric device in all the participants. The mean values of right baPWV and left baPWV are found to be significantly higher in hypertensive subjects compared with obese, diabetic and healthy controls. **Conclusion:** The pulse wave velocity, ASI and pulse pressure serve as independent predictors of cardiovascular mortality and outcomes in hypertension, diabetes and obesity as well as healthy individuals.

Keywords: Arterial stiffness index (ASI), arterial stiffness indices (AS), cardiovascular disease (CVD), diabetes mellitus (DM), hypertension (HTN), obesity, pulse wave velocity (PWV)

Introduction

Cardiovascular diseases (CVD) account for approximately one-third of all deaths and have become a clinical concern worldwide.[1] Elastic arteries, an integral part of cardiovascular system, undergo progressive thickening and lose elasticity over time with age because of increased deposition of collagen, fragmentation and degeneration of elastin, leading to arterial stiffness (AS) or reduced arterial compliance. William Osler stated arterial health as "Man is as old as his arteries," and arterial stiffness is considered as an index of vascular ageing because it reflects both organic and functional stiffness of the arterial wall. Arterial stiffness is a useful predictor and integrated marker of cardiovascular events and mortality.[2,3] Although age-dependent vascular changes occur typically in the fifth decade of life, there is a strong variability of vascular changes between individuals wherein individuals exposed to risk factors present with early vascular changes.

The ejection of blood from the heart produces an arterial pulsation called "pulse wave," and the speed at which it propagates to the periphery is called as pulse wave velocity (PWV). The PWV,

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the gold standard for arterial stiffness is proportional to the rigidity of arterial wall and inversely proportional to the vessel diameter.[4] The primary factor influencing pulse pressure, left ventricular load and cardiac remodeling is an increase in arterial stiffness, which causes the arterial pulse waveform to reflect quickly from the periphery.[5]

Brachial-ankle pulse wave velocity (baPWV) is a measure of systemic arterial stiffness, and carotid-femoral pulse wave velocity (CF PWV) is the reference standard to measure for central arterial stiffness. Arterial Stiffness Index (ASI) is an indirect measure of arterial stiffness.

The incidence of cardiovascular events such as myocardial infraction has been reported to be progressively increasing with age, especially with comorbidities such as hypertension, diabetes and obesity. Arterial stiffness is increased in hypertension even independent od blood pressure levels. Hypertension has been shown to alter properties of vascular smooth muscle cells and promote collagen production causing subsequent increase in arterial stiffness.[6-8] Formation of glycation end products and nitric oxide dysregulation in diabetes mellitus is associated with harmful crosslinking of collagen fibres within the arterial wall leading to accelerated arterial stiffness and increased risk of progression of complications of diabetes mellitus and cardiovascular disease.[9] The prevalence of obesity has increased which is associated with accelerated vascular ageing because of increased levels of LDLs, leading to endothelial dysfunction and thus deposition of minerals such as calcium, which forms patches of plaque.[10] Studies have shown that increased adiposity is associated with higher PWV in obese and hypertensive adults and children.[11] The central systolic blood pressure and pulse pressure being influenced by wave reflection and aortic stiffness are considered to be an independent predictor of arterial stiffness, which is associated with high body mass index (BMI).[12]

There is less knowledge on arterial stiffness indices in adults with comorbidities such as diabetes, hypertension and obesity. Hence, we undertook this study for measuring and comparing the arterial stiffness indices in individuals with comorbidities which may serve as a screening tool in identification of population at risk of cardiovascular diseases and assist in implementation of preventive measures and early treatment in this population.

Objectives

To measure and compare the arterial stiffness indices in healthy adults with diabetes, hypertension and obesity.

Methodology

TYPE of study: Cross-sectional study

A total of 184 adults were evaluated in the age group of 30-50 years, and the participants were divided into 4 groups: Group I (n = 64) (diabetic), group II (n = 40) (hypertensives), group III (n = 40) (obese) and group IV (n = 40) (control).

Exclusion criteria

Pregnant women, individuals with history of COVID-19, people suffering from chronic diarrhea, renal dysfunction, patients with cardiovascular disease, and people with history of smoking were excluded from the study as these factors would affect the arterial stiffness.

After taking approval of institutional Ethics Committee, the study was conducted at AIIMS, Bibinagar in 2022. The study was fully explained, and a written informed consent was obtained from all the participants. Demographic, socio-economic details, medical history, weight and height of the participants were recorded, and body mass index (BMI) was calculated according to standard protocols. Individuals diagnosed as diabetic whose fasting blood sugar (FBS) >130 mg/dl or 7.0 mmol/L, taking insulin or hypoglycemic agents and HBA1C >6, were included in group I, individuals with systolic blood pressure >140 mmHg and DBP > 90 mmHg or on anti-hypertensive drugs included in group II, individuals with BMI>30 (considered as obese as per WHO classification) were included in group III, and healthy adults without any comorbidities were taken as group IV (controls).

The arterial stiffness indices were assessed by using a certified oscillometric device in all the participants. The participants were instructed to avoid alcoholic beverages, large meals, caffeine and smoking within 3 hrs before measurement. The procedure was performed in supine position after seating for 5 minutes. The arm BP cuffs were wrapped 2-3 cm above the cubital fossa, whereas the ankle cuffs positioned 1-2 cm above the superior aspect of the medial malleolus. The central hemodynamic parameters such as central blood pressures (systolic blood pressure (SBP), diastolic blood pressure (DBP), pulse pressure (PP) and heart rate) were measured. The vascular stiffness indices, i.e., left and right side brachial-ankle pulse wave velocity (LbaPWV and RbaPWV), carotid-femoral pulse wave velocity (CF PWV), right and left brachial arterial stiffness index (R bra ASI and L bra ASI) and right and left ankle arterial stiffness index (R Ank ASI and L Ank ASI) were recorded. The normal range of baPWV was defined as <1400 cm/s, elevated arterial stiffness was defined as baPWV >1400 cm/s, and the reference values for normal cfPWV < 760cm/sec and elevated arterial stiffness were defined as >760cm/sec. The normal reference value for arterial stiffness index is 20-70 mmHg.

The collected values of pulse wave velocity and other arterial stiffness indices of participants were compared between the groups to identify the risk of cardiovascular diseases.

Data analysis plan: Statistical analysis

Mean ± standard deviation was calculated for continuous distributed variables. For independent comparison of the continuous and categorical variables of BMI and arterial stiffness between groups, independent sample t-tests were used. Mann-Whitney U test and Kruskal-Wallis test were used to compare the differences in mean parameters across the groups. Data were analyzed with SPPS

software 25. The differences between the groups by analyzing the mean value, standard error and 95% confidence interval by determining the *P* value. All the statistical tests were 2-sided, and $P < 0.05$ was considered statistically significant.

Observation and Results

A total of 186 participants in the age group 30-50 years, 64 diabetic, 40 hypertensives, 40 obese and 40 healthy individuals were recruited for the study, but 6 participants were excluded because they had coexisting hypertension with diabetes.

The socio-economic levels were high in hypertensive and obese individuals and lower in normal healthy subjects. The mean values of central hemodynamic parameters such as SBP, DBP and pulse pressure were significantly higher in hypertensive subjects (46.10 ± 8.37), followed by the diabetes group (43.11 ± 9.09) compared with obese (40.28 ± 6.70) and control groups (40.12 ± 4.54) [Table 1].

The mean values of right baPWV and left baPWV (1451.805 ± 197.023) (1550.630 ± 361.57) [Table 2] [Figure 1] are found to be significantly higher in hypertensive subjects (group II) followed by obese subjects (1275.664 ± 160.6310) (1274.100 ± 140.9192) (group III) and diabetes (1178.861 ± 101.4313) (1199.911 ± 132.0254) (group I) compared with controls (1023.54 ± 121.21) ($P < 0.001$). The systolic and diastolic blood pressure values were found to be high among subjects with high baPWV.

Subjects who were hypertensive were older in age, and the mean age in years was (43.21 ± 6.9) compared with diabetic (39.64 ± 7.83), obese (33.87 ± 6.54) and control groups (32.15 ± 5.83). It was also observed that the no. of females having hypertension had higher baPWV than males.

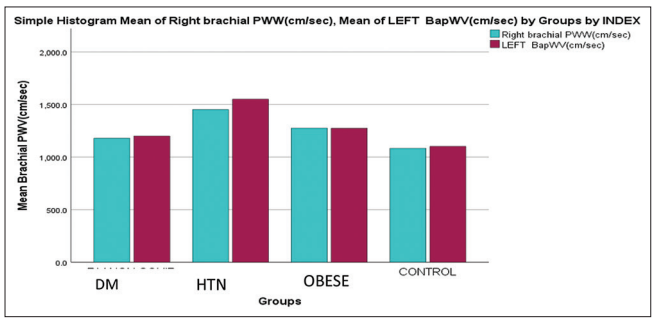

Figure 1: Comparison of means of Right BaPWV and Left BaPWV (cm/s) among different groups

We also observed that the mean BMI of the obese subjects was high (30.81 ± 3.56) and compared with subjects with hypertension (27.92 ± 3.94) and diabetic subjects 26.77 ± 3.0) ($P < 0.001$). The mean values of CF PWV also followed a similar pattern of baPWV with significantly higher values in hypertensive (980.99 ± 209.52) [Figure 2] followed by obese (820.16 ± 122.42) and diabetic subjects (785.05 ± 111.08) compared with controls ($P < 0.001$).

The mean values of the right and left ankle Arterial Stiffness Index (ASI) were found to be significantly higher in subjects with hypertension, followed by obese and diabetes subjects compared with controls, although the values were not statistically significant [Figure 3].

Discussion

We observed in our study that the baPWV and cfPWV are significantly higher in individuals with hypertension compared with subjects with other comorbidities such as diabetes and obesity. The results are in coherence with the results of study performed by Sueng Lee *et al.*[13] We also found that the baPWV were higher in women compared with men, and therefore, women were at higher risk of developing cardiovascular disease. The elevated PWV is an independent predictor of cardiovascular risk.[14] Increased pulse wave velocity is regarded as a marker of asymptomatic organ damage and is considered to be a negative prognostic factor in management of hypertensive patients by European Society of Cardiology.[15] The mean values of pulse pressure and ASI were high in hypertensive subjects in this study when compared with other groups similar to the results in the study performed by Vaccarino *et al.*[16] Increase in ASI and PP are independent measures of vascular ageing and considered as a reflection marking the physiological function of cardiovascular system.

Hence, hypertension is the riskiest factor among other comorbid conditions such as obesity and diabetes for developing cardiovascular disease. The cause-and-effect relationship between arterial stiffness and hypertension is complex, but a consistent temporal sequence of arterial stiffness preceding hypertension was observed in other studies and animal model studies.[17] Elevated blood pressure may cause adverse effect on vascular wall and accelerated arterial stiffening in not only small arteries

Table 1: Comparison of demographic details, BMI and central hemodynamic parameters in various groups

Parameters	Diabetes (Group I) (*n*=64)			Hypertension (Group II) (*n*=40)			Obese (group III) (40)			Control (group IV) (*n*=40)			*P*
	Mean	SD	SE	Mean	SD	SE	Mean	SD	SE	Mean	SD	SE	
Age	39.64	7.83	1.34	43.21	6.9	1.56	33.87	6.54	1.15	32.15	5.83	2.09	0.128
BMI	26.77	3.00	0.56	27.92	3.94	0.88	30.81	3.56	0.71	24.43	2.06	0.94	<0.001
SBP	128.42	10.72	1.86	142.84	12.13	2.90	131.86	11.43	2.03	118.32	9.08	2.07	0.26
DBP	84.93	8.62	2.09	96.41	9.62	1.18	92.05	7.08	1.74	78.63	6.29	1.85	0.01
PP	43.11	9.09	1.71	46.10	8.37	1.87	40.28	6.70	1.34	40.12	4.54	1.87	<0.001

The data is presented as Mean±SD. BMI: Body mass index; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; PP: pulse pressure

Table 2: Comparison of Arterial stiffness indices in various groups

Parameters	Diabetes (Group I) (*n*=64)			Hypertension (Group II) (*n*=40)			Obese (group III) (40)			Control (group IV) (*n*=40)			*P*
	Mean	SD	SE	Mean	SD	SE	Mean	SD	SE	Mean	SD	SE	
R baPWV	1178.8	101.4	19.16	1451.8	197.0	44.05	1275.6	160.63	32.12	1023.54	121.21	21.65	<.005
L baPWV	1199.9	132.0	24.95	1550.63	361.5	80.84	1274.10	140.92	28.18	1065.87	101.23	22.90	<0.001
CFPWV	785.05	111.08	20.99	980.99	209.5	46.85	820.16	122.42	24.48	712.56	106.43	35.23	<0.001
R Bra ASI	27.36	8.74	1.65	30.46	10.00	2.23	28.5	7.87	1.57	26.36	6.75	2.01	0.132
L Bra ASI	26.91	9.58	1.81	30.93	9.72	2.17	27.03	9.39	1.87	23.74	8.34	1.97	0.006
R Ank ASI	38.93	10.23	1.93	47.31	18.16	4.06	37.72	8.32	1.66	37.87	9.03	1.85	<0.001
L Ank ASI	39.96	12.01	2.27	46.97	13.73	3.07	43.94	14.83	1.93	38.78	12.04	1.98	0.008

Data of arterial stiffness indices is presented as Mean±SD; R baPWV & LbaPWV: Right and left brachial ankle pulse wave velocity; CFPWV: Carotid femoral pulse wave velocity; R Bra ASI & L Bra ASI: Right and left brachial arterial stiffness index; R Ank ASI & L Ank ASI: Right and left ankle stiffness index

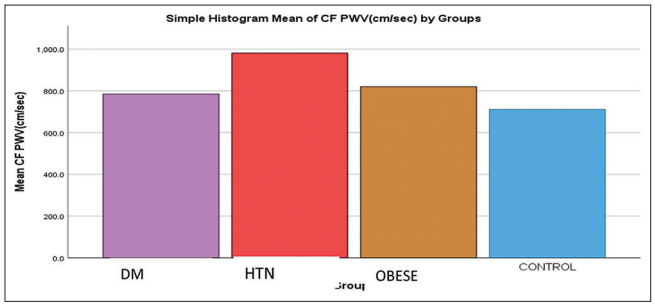

Figure 2: Comparison of mean of carotid femoral PWV among different groups

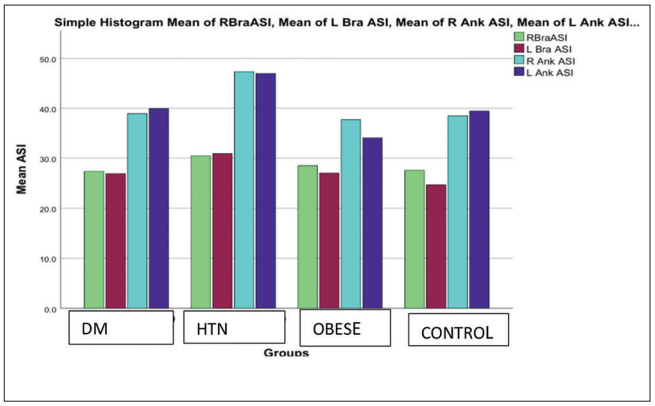

Figure 3: Comparison of mean of R Bra ASI, L Bra ASI, R Ank ASI and L Ank ASI among different groups

and arterioles but also large arteries. However, contrary to this assumption, a recent statement from American Heart Association suggests that arterial stiffness represents a cause rather than consequence of hypertension.[18]

A few longitudinal studies demonstrated that central CF-PWV predicts risk of future cardiovascular events over and above traditional factors.[19,20] An increase in PWV by 1 m/sec corresponds to 15% increase in CVD mortality and events.

We also observed in our study that there was a significant association between individuals with BMI > 30 and arterial stiffness, which is in congruence with the results of the study by Tang *et al*.[20] who indicated that arterial stiffness as measured by baPWV is positively associated with increase in BMI. Hyperinsulinemia and insulin resistance in obesity are linked to reduction in endothelial NO signaling pathway reducing the vasculo-protective effects of NO, leading to endothelial malfunction may be responsible for development of increased vascular stiffness.[21,22]

In the study, the results showed that the baPWV and cfPWV were higher in diabetic subjects than controls. These results are in consensus with some studies, which showed a positive association between arterial stiffness and diabetes.[23] In type 2 diabetes individuals, there is formation of glycation end-products, reduced formation and harmful cross-linking of collagen molecules within the arterial wall, leading to arterial stiffness.[9,24] Increased arterial pulse pressure and pulsatile shear leading to endothelial dysfunction and metabolic dysregulation reduces the nitric oxide bioavailability and increase oxidative stress. Increased sympathetic tone, oxidative stress and reduced nitric oxide bioavailability have also shown to be associated with loss of elasticity and changes in type/structure of elastin and collagen fibres in the arterial wall in diabetes.[25] It is seen that arterial stiffness can be increased even in pre-diabetic populations with impaired glucose tolerance and those with metabolic syndrome well before overt DM.[26,27]

In a community-based population with high prevalence of diabetes, hypertension and obesity, we found in our study that the individuals with comorbidities were significantly associated with increased arterial stiffness as measured by pulse wave velocity. Increased arterial stiffness is closely related to the progression of complications such as nephropathy and retinopathy in hypertensive and diabetes subjects. Thus, early identification and diagnosis of individuals at risk are of clinical importance for early risk assessment, and intervention may provide insight and prevent onset and slow the progress of disease.

Study limitations

There are some limitations in this study. The cross-sectional design of the study did not provide information on the evolution and progression of arterial stiffness indices over time. Although the sample was more representative of the general population, we were unable to trace the evidence of other confounding factors co-existing with DM, despite adjusting for age, BMI and other numerous covariates.

Conclusion

The increased arterial stiffness, central systolic blood pressure and pulse pressure may serve as simple and independent predictors of underlying vascular diseases and strong cardiovascular risk factors in hypertension, diabetes and obesity as well as healthy individuals. However, future work is required to further clarify whether arterial stiffness and pulsatile hemodynamic changes and interventions targeting arterial stiffness are associated with improved clinical outcomes in these conditions.

Ethics approval and consent to participate

The project was started after taking the Institute Ethics committee (IEC) approval (IEC ref no. AIIMS/BBN/IEC/July 2022/163. Written informed consent was obtained from all the participants.

Consent for publication

Taken from IEC and competent authority.

Availability of data and material

The data and the material are saved securely with the investigators accessed with password protection.

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Conflicts of interest

There are no conflicts of interest.

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