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A STUDY OF CORRELATION BETWEEN ARTERIAL STIFFENING AND DNA DAMAGE IN CARDIOVASCULAR DISEASES

Physiology

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ABSTRACT

Arterial stiffening is a significant determinant of cardiovascular diseases. Carotid femoral pulse wave velocity (CF PWV) is a well-accepted tool to measure central arterial stiffening. Previous literatures has shown that increased DNA damage was associated with CVD. It was an observational case control study which consists of CVD patients (n=85) and healthy adults (n=34).Physiological parameters were measured with the Cardiac Risk Profiler. DNA damage was quantified by Cytokinesis block Micronuclei Assay (CBMN).The mean (±SD) values of CFPWV, systolic BP (SBP), peripheral pulse pressure, central aortic systole (Ao systole), central aortic pulse pressure and CBMN frequency showed statistically significant difference between case and control ($p<0.05$). CBMN and CFPWV were the independent risk factors for the development of varying degrees of CVD.

KEYWORDS

Arterial stiffness, DNA damage, cardiovascular diseases

INTRODUCTION

The epidemiological transition in the last few decades has resulted in the rapid rise of CVDs in India[1].The age standardized CVD death rate (272) and disability rate (5438) per one lakh population in India was higher than the global average of CVD death rate (235) and disability rate (4471) per one lakh population[2].Arterial stiffness is a significant determinant of cardiovascular diseases[3,4].Arterial stiffness increase leads to increase of SBP and left ventricular after load, and alteration in DBP and coronary perfusion, which increases the incidence of cardio vascular system related diseases and deaths[5]. Arterial stiffness ensues arteriosclerosis, affecting tunica media due to normal aging or accelerated aging, in preference to atherosclerosis[6]. CVD risk factors accelerate the arterial wall aging, ultimately results in the reduction of compliance of arterial wall and increase of pulse velocity[6]. Elastic arteries are more affected with stiffness than muscular arteries. The CFPWV can be taken as the reference standard for central arterial stiffness measurement[7]. The central and peripheral BP derivatives like systolic and diastolic BP and pulse pressure are impacted by arterial stiffness.

It is accepted that deoxyribonucleic acid (DNA) damage is linked with the development of atherosclerosis which further leads to cardiovascular diseases. These molecular changes affect vessels of the involved part, plaque and circulating cells[8].

So we studied the correlation between DNA damage quantified by CBMN assay (Cytokinesis block Micronuclei) and parameters of arterial stiffness recorded as CFPWV, central SBP , DBP, pulse pressure and peripheral SBP, DBP and pulse pressure.

MATERIALS AND METHOD

It was an observational case control study conducted in the Cardiology Department of Mount Zion Medical College, Kerala. This study consists of 119 subjects which include 85 study subjects with varying degrees of cardiovascular diseases (hypertension, dyslipidaemia, diabetes mellitus, obesity and coronary artery disease) and 34 healthy adult volunteers as control for comparison between groups. Both genders (20 to 60 years) with consent for participation were recruited. Subjects suffering from any chronic illness like renal diseases, cerebrovascular accidents, rheumatic diseases and congenital diseases, and subjects who underwent any invasive procedures for CAD were excluded from the study .The Institutional ethics committee of NIMS university has approved the protocol for the study.

The relevant information and other clinical details were collected using pre-structured questionnaire. Physiological parameters were measured automatically by Periscope of Cardiac Risk Profiler (Genesis Medical Systems Pvt Ltd)[9]. Blood samples were collected for quantification of DNA damage by CBMN assay[10].

Statistical analysis was done using IBM SPSS Statistics 20 Windows (SPSS Inc., Chicago, USA). And summarising the results as mean±SD for all continuous variables and in frequency (percentage) for categorical variables. Mean clinical parameters between study subjects and control subjects were compared by independent sample test. Association between categorical variables and group were assessed by Pearson chi square test. . Pearson correlation coefficients was applied to find the degree of correlation between two continuous measurements. Multivariate logistic regression was applied to find the independent risk factors for CVD. P value <0.05 is considered as statistically significant.

RESULTS

Basic characteristics of study and control subjects, and comparison between them are shown as Table 1. Peripheral SBP, central BP derivatives, CFPWV and CBMN frequency were shown highly significant difference between study subjects with varying degree of cardiovascular diseases and healthy control subjects (p value >0.001). Peripheral DBP and pulse pressure were higher in subjects with varying degree of cardiovascular diseases than healthy controls (p= 0.001).

Table 1 : Characteristics of subjects and Comparison between study and control subjects

Variable	Study subjects	Control subjects	P value
Age (years)	47.20±9.177	39.91±10.370	.0001
Male / female (n/n)	57/28	19/15	0.252*
Peripheral SBP (mmHg)	130.67±16.36	116.79±9.26	.0001
Peripheral DBP (mmHg)	83.34±9.14	77.26±7.23	.001
Peripheral Pulse pressure (mmHg)	47.22±10.42	40.32±7.458	.001
Central Ao SBP (mmHg)	116.49±17.065	100.94±9.28	.0001

Central Ao DBP (mmHg)	81.74±9.007	74.62±5.90	.0001
Central Ao pulse pressure (mmHg)	34.48±9.357	25.56±6.287	.0001
CF PWV (cm/sec)	1223.89±350.029	913.97±180.225	.0001
CBMN frequency(n)	12.88±1.187	10.088±1.215	.0001

Abbreviations : SBP, systolic blood pressure; DBP, diastolic blood pressure; Ao SBP, aortic systolic blood pressure, Ao DBP, aortic diastolic blood pressure; CFPWV, carotid femoral pulse

wave velocity; CBMN, Cytokinesis block Micronuclei.
*Chi-square test

Table 2 Correlation between CBMN frequency and physiological variables included in the study among study subjects

Study subjects	CBMN frequency	
	r (Pearson's correlation Coefficient)	P value
Age	0.246	0.023
Peripheral SBP(mmHg)	0.359	0.001
Peripheral DBP (mmHg)	0.210	0.054
Peripheral pulse pressure (mmHg)	0.387	0.0001
Central Aortic SBP (mmHg)	0.349	0.001
Central Aortic DBP (mmHg)	0.207	0.057
Central Aortic pulse pressure (mmHg)	0.401	0.0001
CF PWV (cm/sec)	0.232	0.033

Abbreviations : SBP, systolic blood pressure; DBP, diastolic blood pressure; Ao SBP, aortic systolic blood pressure, Ao DBP, aortic diastolic blood pressure; CFPWV, carotid femoral pulse wave velocity; CBMN, Cytokinesis block Micronuclei.

The bivariate relation between genetic (CBMN frequency) and physiologic parameters of study subjects were shown as table 2. Physiological parameters such as age, peripheral SBP and pulse pressure, central SBP and pulse pressure and CFPWV were positively correlated with CBMN frequency in the subjects with varying degree of cardiovascular disease. Non-significant correlation between peripheral and central DBP with CBMN frequency were also seen in them.

Table 3 Multivariate logistic regression (7th step) to find out the independent risk factor for the development of CVD

Variable	Odd's ratio	95% confidence interval		P value
		Lower	Upper	
CFPWV	1.003	1.000	1.006	0.023
CBMN	4.090	2.344	7.136	0.000

Abbreviations : CFPWV, carotid femoral pulse wave velocity; CBMN, Cytokinesis block Micronuclei.

Multivariate logistic regression (Table 3) was done to find out the independent risk factor. CFPWV and CBMN were the independent risk factors for the development of varying degrees of CVDs in this study.

DISCUSSION

In this subjects with varying degree of CVDs had significantly higher ($p<0.001$) peripheral SBP, central SBP, DBP and PP, CFPWV and CBMN frequency than the non CVD healthy control subjects. Stephane Laurent et al reported when the arterial stiffness increases, reflected waves return in late systole, so the central PP increases, ventricular load increases, ejection fraction decreases and oxygen demand by myocardium increases and ischemia develops in the sub endocardial area. And considered CFPWV and peripheral PP as markers of arterial stiffness, cardiovascular morbidity and mortality[11].

Similar to this study, Blacher et al found CFPWV was higher in subjects with atherosclerotic alterations than those don't have atherosclerotic alterations (p value 0.0001). Atherosclerotic alterations group also showed high PP. Arterial stiffness increases the shear stress and pressure inside the lumen, which leads to endothelial dysfunction, vascular remodelling, increased collagen production, and speed up the atheroma formation and atherosclerosis progression[13].

Matej Durik et al found cumulative DNA damages aid vascular dysfunction with a rapid progression in human and animal models than mice, and contribute to the incidence of CVDs[14]. CAD patients showed significantly elevated levels of DNA damage in the blood leukocytes[15]

In this study CBMN frequency had showed significant positive correlations with age, peripheral and central SBP, cfPWV ($p<0.05$) and highly significant positive correlations with central and peripheral PP ($p<0.001$). Similar to this study, Jiju et al found a significant association between arterial stiffness and lymphocyte DNA damage in patients with cardiometabolic syndrome[10].

CONCLUSIONS

In the present study, the arterial stiffness parameters and DNA damage quantified by CBMN assay in peripheral lymphocytes were shown significant difference between the study subjects and the control subjects, and DNA damage quantified was correlated with arterial stiffness parameters except peripheral and central DBP in study subjects with varying degree of CVDs. CBMN and CFPWV were the independent risk factors for the development of varying degrees of CVDs .

Our findings have demonstrated the involvement of physiologic and genetic factors for the initiation and development of CVDs.

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