Original Article

Association of level of cognition with sympathovagal imbalance and cardiovascular risks in prehypertension

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Abstract

Background and Aim: Prehypertension is more prevalent in young age group. In India, the prevalence of prehypertension varies from 24.5% to 27.2%. In midlife, blood pressure levels of prehypertension range may have an influence on memory. However, the degree of cognitive decline and its mechanisms in prehypertension is lacking. The aim of the present work is to study the association of the level of cognition with sympathovagal imbalance (SVI) and cardiovascular (CV) risks in prehypertension.

Methods: Eighty-four participants (42 normotensives and 42 prehypertensives) aged between 18 and 44 years were included in this case–control study. The demographic, anthropometric, basal CV parameters, heart rate variability, cardiovascular autonomic function tests (CAFTs), rate pressure product (RPP) as the indicator of CV risk, and event-related potential P300 as the marker of cognitive function, and biochemical parameters of insulin resistance (IR), inflammation, and oxidative stress were recorded. Association of level of cognition with various factors was assessed by Pearson's correlation analysis.

Results: The basal CV parameters were significantly elevated, and total power was reduced in prehypertensives. In CAFTs, 30:15 ratio and Δ DBP_{IHG} were increased, and E: I ratio was decreased in prehypertensive group. The latency of P300 was not significantly prolonged in prehypertensives. Although the correlation was not significant between P300 latency and low frequency: high frequency ratio (the marker of SVI), it was significant with RPP in prehypertensives. The fasting blood glucose, insulin, and homeostatic model assessment-IR were not significant, and high-sensitivity C-reactive protein was elevated; oxidant status was increased and antioxidant status was decreased in prehypertensive groups.

Conclusion: Although prehypertensives have SVI and increased CV risks, considerable memory impairment was not found in them. However, the level of cognition was linked to CV risks.

Key words: Cognitive deficit, insulin resistance and oxidative stress, prehypertension, sympathovagal imbalance

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INTRODUCTION

The Seventh Report of the Joint National Committee (JNC-7) on detection, evaluation, and treatment of high blood pressure (BP) introduced the term "prehypertension" and set the cutoff value of systolic BP (SBP) as 120–139 mmHg and/or diastolic BP (DBP) as 80–89 mmHg.[1] Prehypertension is more prevalent in young age group. A meta-analysis report of cross-sectional studies has shown that the overall prevalence of prehypertension as 38%. Out of

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which, non-Asian population has higher prevalence compared to Asians.[2] In India, the prevalence of prehypertension varies regionally from 24.5% to 27.2% in Himachal Pradesh. High SBP contributes to ischemic stroke and lacunar infarct and results in reduction in white-matter density possibly leading to impaired cognitive functioning, especially of executive functions.[3] Although hypertension is an established risk factor for cognitive deficit, the role of prehypertension as a risk factor for cognitive deficit is not yet studied.[4] The term cognitive decrements or deficit is defined as an average cognitive performance at around the 35th to 45th percentiles of normative data affecting one or multiple domains of cognition; though the cutoff to detect cognitive deficit is at 5th to 10th percentile.[5] The event-related potential, i.e., P300 can serve as better tool for assessing cognitive deficit as P300 is closely related to cognition-related brain functions such as attention, intelligence, and working memory.[6-10]

Cognition is closely related with autonomic functions.[11] Recently, we have reported from our laboratory that the physiological basis for sympathovagal imbalance (SVI) in prehypertension is due to withdrawal of vagal tone and sympathetic overactivity.[12,13] Further, we have found metabolic derangements are contributors to SVI in prehypertension.[14,15] However, there is a paucity of literature in revealing the association of autonomic imbalance and metabolic derangements with cognitive decline in prehypertensives in Indian population. Furthermore, in these studies, cognitive functions have not been studied objectively in Indian population. Therefore, our study was designed to assess the association of SVI, insulin resistance (IR), and oxidative stress with the level of cognition in prehypertensives.

MATERIALS AND METHODS

This case–control study was conducted after receiving approval from the Jawaharlal Institute of Postgraduate Medical Education and Research (JIPMER) Scientific Advisory Committee and Institute Ethics Committee for human studies. This study was conducted in the autonomic function testing laboratory and electrophysiology (EP) laboratory, Department of Physiology, JIPMER. The participants were recruited from medicine outpatient department of JIPMER.

Sample size calculation

Total sample size was calculated to be 84 participants (42 controls and 42 prehypertensives). The objective of this study was to measure and compare the low frequency-high frequency (LF-HF) ratio with P300. Therefore, considering the mean and standard deviation (SD) values of LF-HF ratio, accepting power as 80%, and keeping the level of significance 5% using previous reference,[16] the total sample size calculated by OpenEpi software was 84.

Estimation of biochemical parameters

Written informed consent was obtained, and 5 ml of fasting blood sample was collected from all the participants. Fasting blood glucose (FBG) was estimated by oxidation–reduction method using glucometer (Accu-chek Performa, Roche Diagnostics; Sweden). The serum insulin was estimated using ELISA kit from Chemux BioScience, Inc., CA, USA and homeostatic model assessment-IR (HOMA-IR) is computed from the formula, HOMA-IR = fasting serum insulin (μU/ml) × FBG (mg/dl)/405. The inflammatory marker high-sensitivity C-reactive protein (hsCRP) was done using ELISA kit from Calbiotech, Inc., CA, oxidative stress markers were assayed using QuantiChrom™ thiobarbituric acid reactive substances (TBARS) assay kit from bioassay systems, CA to detect oxidant status, and QuantiChrom™ Antioxidant assay kit from bioassay systems, CA to detect antioxidant status.

Inclusion criteria

Based on JNC-7 classification (1), the participants were divided into:

- Normotensives (n = 42): SBP 100–119 mmHg and DBP 60–79 mmHg, healthy person
- Prehypertensives (n = 42): SBP 120–139 mmHg and DBP 80–89 mmHg, in otherwise healthy participants.

Exclusion criteria

1. Participants having any acute illness or receiving any medications
2. Participants practicing regular sports/athletic activities
3. History of smoking, alcoholism, endocrinal disorder, cardiovascular (CV) disease, neurological disorders, and renal disorders.

Recording of anthropometric and basal cardiovascular parameters

Participants were asked to report to Autonomic Function Laboratory of Physiology Department at about 9 am following a light breakfast. After obtaining the informed consent, anthropometric parameters were recorded.

Omron (SEM 1 Model), the automatic BP monitor (Omron Healthcare Co., Ltd., Kyoto, Japan), was used to measure BP in sitting position. The cuff size of the equipment was 121 mm (width) × 446 mm (length) and cuff tube length was 600 mm. The BP cuff was tied on the arm approximately 2 cm above the cubital fossa, and care was taken that the cuff was neither too tight nor loose.

For each participant, SBP, DBP, and basal heart rate (BHR) were recorded at an interval of 5 min in each arm twice, and the mean of the 4 recordings was considered for each parameter. Rate pressure product (RPP) was computed using the following formula: RPP = SBP × heart rate × 10^{-2}.[17]

Recording of heart rate variability

After 15 min of supine rest, electrocardiogram (ECG) was recorded for 5 min for short-term heart rate variability (HRV) analysis following the guidelines of task force.[18] ECG electrodes were connected, and lead II ECG was acquired at 500 samples per second for each channel using PowerLab 8/30 ML 870 data acquisition system with LabChart Pro software. The acquired 5 min resting lead II ECG (filtered with bandpass filters) was carefully analyzed for ectopic and artifacts, which were meticulously removed manually. The detection of R-waves was done with a thresholding algorithm of LabChart Pro software. From the RR tachogram, power spectral analysis was performed by FFT. Time-domain parameters (root mean squared successive difference [RMSSD], standard deviation of normal to normal interval [SDNN], NN50, and pNN50) and frequency domain parameters (total power [TP] of HRV, normalized LF power [LFnu], normalized HF power [HFnu], and ratio of LF-HF ratio power) were computed using HRV analysis software (Kubios HRV, version 2.2 Finland).

Recording of P300 event-related potential

Cognitive event-related potential, i.e., P300 was recorded in the context of a standard auditory oddball paradigm in the EP laboratory of Department of Physiology, JIPMER using Nihon Kohden EP/electromyography (EMG) machine. The recommendation of the International Federation of Clinical Neurophysiology was used,[19] and as per the protocol of recording in Indian laboratory setup.[20] The participants were instructed to come with cleaned oil-free scalp. Ear wax was ruled out and 10 min of rest was given before recording. The scalp of the participant was cleaned with spirit, and the electrode placements were done according to the 10–20 international system of EEG.[19]

The active, reference, and ground electrodes were connected to channel 1 preamplifier with an impedance of ≤2 kΩ. The midpoint between both the tragus and the midpoint between nasion and occipital protuberance were marked. At the point of intersection of above midpoints, active recording electrode Cz (central zero point on scalp) was placed. With the help of jumper electrode, two reference electrodes were placed one on each mastoid. The ground electrode was placed in forehead Fz near to the hairline. The electrodes used were made of Ag-AgCl. The bandpass filter range was kept at 0.1 Hz and 50 Hz. Through a headphone, auditory stimulus was given binaurally.

The participants were asked to relax totally and asked to concentrate on the rare stimulus. The stimulus intensity was kept at 40 dB with the "tone" as the target or rare stimulus and "click" as nontarget or frequent stimulus. The stimulus frequency for tone burst and click were kept at 2000 Hz and 1000 Hz, respectively. The click duration was set at 0.1 ms. The stimulus occurrence speed was kept at 1 stimulus per second. The participants were asked to open their eyes and fix to a point to avoid alpha waves in EEG.

The rare stimuli were applied randomly, and the percentage of rare stimuli was set at 20% and frequent stimuli at 80% of random. The stimulation rate was 0.5 Hz/s. The number of stimuli to be given was preset at 30. The signals were picked by electrodes, filtered, amplified, averaged, displayed, and analyzed using Neuropack software on the screen of Nihon Khoden EP/EMG machine.

N1 was the negative wave at 100 ms, N2 was the negative wave at 200 ms, P2 was the positive wave at 200 ms, and P3 was the positive wave at 300 ms. Among these waves, P300, i.e. the positive wave at 300 ms, was considered as the marker of cognition. The procedure of recording was repeated for reproducibility of P300, and the marking was done for the latencies of N1, P2, N2, and P300 in milliseconds and the amplitudes of N1-P2, P2-N2, and N2-P3 in microvolts.

Statistical analysis of data

Statistical analysis was performed by GraphPad InStat and SPSS software version 19 (SPSS; SPSS Inc., Chicago, IL, USA) for Windows. The data were subjected to Kolmogorov–Smirnov normality test. All the data were expressed as mean ± SD The association of P300 with CV and biochemical parameters was assessed by Pearson's correlation analysis.

RESULTS

No significant difference was observed in age ($P = 0.4548$) in control and prehypertensive group [Table 1]. Body weight, BHR, and RPP were significantly increased in prehypertensives compared to controls; BMI was not significantly increased [Table 1]. On analysis of the frequency domain and time domain parameters of short-term HRV, TP was significantly reduced among the prehypertensives ($P = 0.0235$) compared to the controls. When the absolute powers were expressed in normalized units, LFnu was significantly elevated and HFnu was depressed in prehypertensives ($P < 0.0001$)

Table 1: Comparison of demographic, anthropometric, basal cardiovascular parameters, short-term heart rate variability, and cardiovascular autonomic function test parameters between control and prehypertensive groups

Parameters	Controls (*n*=42)	Patients with prehypertension (*n*=42)	*P*
Age (years)	30.19±5.01	29.30±5.82	0.4548
Body weight (kg)	64.12±10.68	70.41±11.33	0.0105
Height (m)	1.62±0.10	1.67±0.07	0.0095
BMI (kg/m^2)	24.34±2.81	25.16±3.59	0.2471
BHR (bpm)	73.24±10.58	77.42±8.38	0.0480
SBP (mmHg)	111.88±7.98	130.02±5.84	<0.0001
DBP (mmHg)	68.48±6.19	85.83±2.90	<0.0001
RPP (mmHg/min)	81.96±13.57	100.67±11.82	<0.0001
FDI parameters			
TP (ms^2)	1054.64±734.05	756.26±403.23	0.0235
LFnu	40.54±16.27	55.88±14.90	<0.0001
HFnu	59.46±17.13	44.11±14.90	<0.0001
LF-HF ratio	0.82±0.54	1.53±0.89	<0.0001
TDI parameters			
SDNN (ms)	46.20±19.61	29.05±9.31	<0.0001
RMSSD (ms)	64.53±24.67	38.06±20.42	<0.0001
NN50	50.35±21.08	38.07±12.27	0.0016
pNN50 (%)	30.83±13.65	23.02±8.16	0.0021
CAFT parameters			
30:15 ratio	1.21±0.29	1.30±0.25	0.9814
E: I ratio	1.39±0.17	1.34±0.30	0.3501
ΔDBP_{IHG}	19.30±5.22	24.88±6.41	<0.0001

Values expressed as mean±SD; Analysis done by Student's unpaired *t*-test. *P*<0.05 was considered statistically significant. BMI: Body mass index, BHR: Basal heart rate, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, RPP: Rate pressure product, TP: Total power, LFnu: Low-frequency component expressed as normalized unit, HFnu: High-frequency component expressed as normalized unit, LF-HF ratio: Ratio of low-frequency power to high-frequency power of heart rate variability, SDNN: Standard deviation of normal to normal interval, RMSSD: Square root of the mean squared differences of successive normal to normal intervals, NN50: The number of interval differences of successive NN intervals >50 ms, pNN50: The proportion derived by dividing NN50 by the total number of NN intervals, 30:15 ratio: Ratio between maximum RR-interval at 30th beat and minimum RR interval at 15th beat, E: I ratio: Ratio of longest RR interval during expiration to the shortest RR interval during inspiration averaged over 6 cycles of respiration, ΔDBP_{IHG}: Difference in diastolic blood pressure between supine and isometric hand grip, CAFT: Cardiovascular autonomic function test

when compared to controls. The LF-HF ratio was significantly elevated in prehypertensives ($P < 0.0001$) compared to controls [Table 1]. The analysis of the time domain parameters revealed that there was a highly significant decrease in RMSSD ($P < 0.0001$) and SDNN ($P < 0.0001$) among prehypertensives compared to controls. pNN50 ($P = 0.0021$) and NN50 ($P = 0.0016$) were significantly reduced in prehypertensive group compared to controls [Table 1].

There was a significant increase in ΔDBP_{IHG} ($P < 0.0001$) during isometric handgrip and no significant reduction in E: I ratio ($P = 0.3501$) and 30:15 ratio ($P = 0.9814$) in prehypertensive group compared to control group. The P300 latency ($P = 0.8360$) was not significantly prolonged in prehypertensives compared to controls [Table 2]. Although the amplitude of P300 wave is decreased in prehypertensives, the difference was not statistically significant ($P = 0.5865$). Prehypertensives do not show significantly elevated FBG ($P = 0.1924$), insulin ($P = 0.3516$), and HOMA-IR ($P = 0.1782$) values compared to controls [Table 3]. There was a significant elevation of hsCRP ($P < 0.0001$) and TBARS ($P = 0.0248$) in prehypertensive group compared to control group. The total antioxidant status (TAS) ($P = 0.0011$) was reduced in prehypertensive group compared to controls.

Table 4 shows the correlation of P300 with various important parameters such as BMI, RPP, FBG, Insulin, HOMA-IR, TBARS, hsCRP, and LF-HF ratio of control and prehypertensive groups. There was no significant positive correlation with prehypertensive group when compared to control group.

DISCUSSION

As P300 assessed by event-related potential is an established marker of higher cognitive function. In the present study, we observed no significant prolongation of P300 latency in prehypertensives [Table 2]. However, there was a prolongation of N100 and P200. These findings indicate, though there was a tendency toward memory loss, the cognitive impairment was not prominent in these participants, which does not corroborate with the other reports.[2] Previous studies have reported that the primary pathophysiology involved in elevated BP in prehypertensive is the SVI.[13-15] In the present study, LF-HF ratio, the indicator of SVI or sympathovagal balance was significantly elevated in prehypertensives [Table 1]. LF-HF ratio of resting HRV is the index of sympathovagal balance, and increase in this ratio depicts SVI with sympathetic accentuation and vagal inhibition, and a decrease in the ratio depicts SVI with vagal accentuation and sympathetic reduction.[18,21] Thus, significantly high LF-HF ratio in prehypertensives compared to controls indicates the presence of substantial SVI in prehypertension.

LFnu, the indicator of sympathetic cardiac drive, was significantly elevated in prehypertension when compared to controls [Table 1]. HFnu, the marker of parasympathetic cardiac drive, was significantly declined in prehypertensives compared to controls [Table 1]. Thus, a decrease in HFnu depicts decreased vagal activity in prehypertension and patients with hypertension. Thus, these findings suggest that SVI in prehypertension was due to sympathetic excitation and parasympathetic

Table 2: Comparison of P300 latency and amplitude between control and prehypertensive groups

Parameters	Controls (*n*=42)	Patients with prehypertension (*n*=42)	*P*
N100 (ms)	107.71±11.77	115.93±18.31	0.0165
P200 (ms)	194.95±26.62	201.95±30.23	<0.0001
N200 (ms)	231.76±25.70	234.05±30.68	0.7117
P300 (ms)	341.57±44.56	343.45±38.17	0.8360
N1-P2 (μv)	8.07±5.75	7.79±5.35	0.8179
P2-N2 (μv)	3.60±2.42	3.18±2.85	0.4687
N2-P3 (μv)	12.03±4.92	11.40±5.63	0.5865

Values expressed as mean±SD; Analysis done by Student's unpaired *t*-test. *P*<0.05 was considered statistically significant. N100 (N1): Negative wave that appears in 100 ms from application of stimulus in ERP tracing, P200 (P2): Positive wave that appears in 200 ms from application of stimulus in ERP tracing, N200 (N2): Negative wave that appears in 200 ms from application of stimulus in ERP tracing, P300 (P3): Positive wave that appears in 300 ms from application of stimulus in ERP tracing. ERP: Event-related brain potential, SD: Standard deviation

Table 3: Comparison of biochemical parameters between control and prehypertensive groups

Parameters	Controls (*n*=42)	Preypertensives (*n*=42)	*P*
FBG (mg/dl)	79.09±9.59	81.64±8.13	0.1924
Insulin (μU/l)	7.48±2.98	8.15±3.55	0.3516
HOMA IR	1.47±0.63	1.69±0.84	0.1782
hsCRP (mmol/l)	2.24±1.92	4.14±2.28	<0.0001
TBARS (μM)	1.03±0.73	1.49±1.08	0.0248
TAS (μM)	419.23±130.68	331.16±106.09	0.0011

Values expressed as mean±SD; Analysis done by Student's unpaired *t*-test. *P*<0.05 was considered statistically significant. FBG: Fasting blood glucose, HOMA-IR: Homeostasis model assessment of insulin resistance, hsCRP: High-sensitivity C-reactive protein, TBARS: Thiobarbituric acid reactive substance, TAS: Total antioxidant status, SD: Standard deviation

Table 4: Correlation of P300 with various important parameters of control and patients with prehypertension groups

Parameters	Controls (*n*=42)		Patients with prehypertension (*n*=42)	
	r	*P*	*r*	*P*
BMI	0.092	0.148	0.210	0.075
RPP	0.167	0.112	0.262	0.045
FBG	0.032	0.256	0.202	0.098
Plasma insulin	0.076	0.190	0.197	0.102
HOMA-IR	0.040	0.282	0.256	0.058
TBARS	0.030	0.257	0.200	0.078
hsCRP	0.080	0.162	0.195	0.101
LF-HF ratio	0.160	0.117	0.206	0.078

The *P*<0.05 was considered significant. P300: Positive wave at 300 ms in event-related potential tracing, BMI: Body mass index, RPP: Rate pressure product, LF-HF ratio: Ratio of low frequency to high frequency power of heart rate variability, hsCRP: High-sensitivity C-reactive protein, TBARS: Thiobarbituric acid reactive substances, HOMA-IR: Homeostasis model assessment of insulin resistance, FBG: Fasting blood glucose

inhibition. LF-HF ratio was not significantly correlated with P300 in prehypertensive and control groups [Table 4]. Thus, findings of the present work indicate the there is no close link of SVI with memory loss in prehypertension.

Although hypertension has long been known to cause impairment in cognitive function,[22-25] a recent report has indicated cognitive loss in prehypertension.[2] Prehypertension affects both peripheral and central arteries and results in stiffening and vascular remodeling. There are reports showing the impairment of endothelial progenitor cells in affecting endothelial-repairing capacity *in vivo* in prehypertensives compared to normotensives. Although blood flow to the brain remains unchanged over a larger range of BP fluctuations, in long-standing cases of prehypertension, there is derangement in autoregulation. This increases the susceptibility to vascular stress along with the formation of aneurysm predisposing to brain ischemia and infarction. These changes may cause cognitive impairment in prehypertension. However, there are no reports showing the association of vascular dysfunctions and cognitive deficit in young prehypertensives from the Indian subcontinent. Therefore, in this present work, we have tried to study the plausible pathophysiology of cognitive loss in prehypertension.

All the time-domain indices of HRV (RMSSD, SDNN, NN50, and pNN50) were significantly reduced in prehypertensive groups compared to control group [Table 1] demonstrating that parasympathetic autonomic modulation was considerably less in prehypertensives as time-domain indices indicate cardiac vagal drive.[18,21] Further, this was supplemented by reduced HFnu and TP of HRV [Table 1]. As discussed above, HFnu of HRV is the indicator of vagal drive to the heart, and TP reflects the overall power of vagal cardiac regulation.[26] Thus, these findings represent decreased vagal drive of cardiac autonomic control in prehypertensives. Significant increase in Δ DBP_{IHG} in prehypertension indicates increased sympathetic reactivity in these participants, as Δ DBP_{IHG} represents sympathetic reactivity.[27] Thus, autonomic imbalance in prehypertension is owing to augmented sympathetic activity as well as reactivity and diminished vagal activity as well as reactivity.

Furthermore, the BHR was significantly more in prehypertensives compared to controls [Table 1] indicating the poor vagal tone in these individuals, as resting tachycardia indicates decreased vagal tone.[28,29] Resting tachycardia more than 75 beats/min is a CV risk and has been reported to be linked with CV mortality and morbidity.[29]

Prehypertensives had significantly increased RPP compared to normotensives [Table 1]. RPP is a

determinant of myocardial oxygen consumption and raised RPP depicts myocardial work stress. Thus, the findings of the present work show cardiac stress in prehypertension, which is a CV risk. Further, TP of HRV was significantly declined in prehypertensive groups compared to control group [Table 1]. Decreased TP that depicts reduced HRV has been documented to be associated with all-cause mortality and sudden cardiac death. Thus, resting tachycardia increased RPP and decreased TP in prehypertension indicate considerable CV risks in these participants.

There are reports of metabolic derangements in prehypertension.[12] There is also a report of decline in cognitive function in conditions of metabolic derangements such as dyslipidemia, IR, and oxidative stress.[30] However, there are no reports demonstrating cognitive impairment in prehypertension in Indian population. Furthermore, there are no reports on cognitive status in prehypertension. In the present study, fasting blood sugar, insulin, and HOMA-IR were not significantly increased in prehypertensives compared to controls. Although IR has also been strongly implicated in the development of cognitive impairment in Alzheimer's disease,[31] in the present study, levels of FBG, insulin, and HOMA-IR were not significantly high in prehypertensives compared to controls [Table 3]. This could be due to moderate sample size and relatively younger age group.

Another linking mechanism of cognitive impairment in prehypertension could be the oxidative stress, as level of TBARS was significantly increased in prehypertensive group compared to control groups [Table 3]. Further, TBARS was significantly correlated with P300 in prehypertensive group [Table 3], and TBARS had a significant independent contribution to P300 in prehypertension [Table 4]. Recently, oxidative stress has been linked to autonomic imbalance,[32] and we have reported the association of oxidative stress with SVI in prehypertension.[16] Further, in the present study, TBARS was significantly correlated with LF-HF ratio in prehypertensive group [Table 4]. Furthermore, TAS was considerably reduced in prehypertension. Therefore, it appears that the SVI could be the pathophysiological link between oxidative stress and cognitive deficit in prehypertension. Although hsCRP was significantly more in prehypertensives, it was not correlated with P300 in these participants. Therefore, hsCRP is unlikely to contribute to memory loss in these participants.

Although the exact cause of cognitive loss is not known, few reports have suggested that cognitive decline in hypertension could be due to cerebrovascular damage. The connection of the frontal lobes to other cortical and subcortical structures such as limbic system is disrupted in white matter tract injuries that have a profound influence on autonomic functions.[11] However, the role of autonomic dysfunction-affecting cognition has not been studied in prehypertension.

Although we could not establish a positive link with cognitive deficit and prehypertension, chronic SVI with sympathetic accentuation has been reported to cause hypertrophy of vascular wall with narrowing of vessel lumen causing decreased cerebral perfusion,[33-35] which might contribute to the cerebrovascular component of cognitive impairment and also could be the physiological basis for nonvascular mechanisms. The difference could be due to relatively younger age group in the present study compared to middle-aged and elderly participants recruited in the study of Chen *et al*.[2] Therefore, future studies with large sample size should investigate the cerebrovascular profile of SVI in prehypertension.

Limitations of the study

The major limitation of the study is the modest sample size that might not have been enough to support the statistical analysis of data for yielding cognitive deficit. Furthermore, we have not conducted questionnaire tests for the assessment of cognitive functions.

CONCLUSION

We conclude that prehypertensives have SVI (in the form of sympathetic overactivity and decreased vagal modulation) and increased CV risks. Their level of cognition was linked to CV risks. However, the memory impairment was not significant in prehypertensives.

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Conflicts of interest

There are no conflicts of interest.

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