

A study of cognitive function in recently diagnosed essential hypertensive patients

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Abstract:

Essential Hypertension is considered as an important independent risk factor for decline cognitive function leading to dementia and stroke. We assess cognitive function of newly detected patients of essential hypertension over 45 years of age. This cross-sectional study includes 62 hypertensive (stage 1 and 2) cases. Data was collected through interview and investigations. Cognitive function was measured by minimental status examination scale. The MMSE score among hypertensive patients ranges from 14 to 28 and mean score was 22.03 (SD 2.10). SBP, DBP and age shows a significant negative effect on MMSE score ($p < 0.01$). The Score of various cognitive domains on MMSE scale was not significantly different in stage 1 and stage 2 hypertensive patients. The cognitive function decreases significantly with increasing age in hypertensive patients ($p < 0.05$). Measuring the cognitive function in newly detected essential hypertensive patients may have important health implication, as cognitive function along with WML are considered as a prognostic factor for stroke and early marker of brain damage

Key word: Essential Hypertension, Systolic blood pressure, Diastolic blood pressure, Cognition

INTRODUCTION:

Globally, hypertension ranks third risk factor for poor health resulting in 13% of total deaths, whereas in developing countries, hypertension ranks eighth among risk factor for poor health.¹ South East Asian people are at most risk of hypertensive diseases, probably because of higher fat deposit at lower BMI, when compared to their western counterpart. The prevalence of

hypertension in adults in India is showing increasing trends, i.e. from 0.25 in 1960 to 7.08 in 1995.^{2,3,4,5}

It is well known that hypertension is a risk factor for cerebrovascular disease. Hypertension causes arteriosclerosis causing partial and/or complete small vessel occlusion resulting in silent cerebral white matter lesions (WML) with associated cognitive impairment, progressing to dementia and /or stroke.^{6,7,8,10,11} Framingham heart study⁸ provided the first clear evidence of relationship between hypertension and cognition in aging population. The inverse relation of hypertension and specific cognitive functions is already established in the western countries.^{6,7,8,9}

Considering the increasing prevalence of hypertension at relatively younger age in Indians; we conducted this study to find out the association of essential hypertension with cognitive function in newly diagnosed hypertensive patients over 45 years of age.

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MATERIAL and METHODS:

A cross-sectional study was conducted in tertiary care teaching hospital in Central India. Study participant comprises of recently diagnosed hypertensive patients (hypertension stage 1 and stage 2 as per the JNC VII criteria) and not yet started on antihypertensive treatment. Persons with secondary hypertension, taking antihypertensive treatment, known case of diabetes mellitus were excluded. Attempts were made to include only new cases (incident cases) of hypertension. If the person have increased carotid intima media thickness, albuminuria, hypertensive retinopathy, left ventricular hypertrophy or having clinical evidence of cerebrovascular disease and/or target organ damage like coronary heart disease, cardiac failure, and/ or renal impairment were excluded from the study. The study protocol was approved by the Institutional Ethical Committee.

Sample size of 62 was calculated at 5% significance level (), with precision of 20% and considering prevalence of impaired cognition in hypertensive's to be 40%.

Data was collected using pre-designed structured interview schedule. The interview schedule was pilot tested and final schedule included question on socio demographic information, presenting complaints and history, clinical examinations and investigations like blood sugar, urine examination, renal function test, ECG, serum electrolytes, lipid profile, fundus examination, USG – KUB, carotid doppler and minimental status examination scale (MMSE) for cognitive function. Persons over 45 years of age attending tertiary care center were subjected to blood pressure measurement. Those with hypertension, not on antihypertensive medication were included in the study as cases after informed consent. Complete socio-demographic information, presenting complaints were recorded. Participants were examined and later on subjected to necessary investigations.

Blood pressure was measured by mercury sphygmomanometer. The individuals were made comfortable and seated for at least for five minutes before measurement. Pressures at which

sound appeared and muffled or disappeared were taken as a systolic blood pressure (SBP) and diastolic blood pressure (DBP) respectively. The measurement was made with individual in sitting position. Two readings were taken half an hour apart and the average of two was taken as a final reading.¹² As per the JNC VII¹³ blood pressure was classified as normal (SBP<120 and DBP<80 mm of Hg), pre-hypertensive (SBP = 120-139 and DBP = 80-89 mm of Hg), Stage I hypertension (SBP = 140-159 and DBP = 90 - 99 mm of Hg), stage II hypertension (SBP>160 and DBP>100 of Hg).

Body weight, height and Body Mass Index (BMI) were measured as per the procedure specified in WHO Technical Report Series (1995) No 854¹³. Smokers were classified as current smokers, past smokers, and nonsmokers. Past smokers were those who quit smoking for at least 1 year at the time of Study. Current-smokers were defined as those who are currently smoking any number or any from of tobacco. Alcohol intake was categorized as regular intake (almost daily), irregular (social) drinker, or never.

Cognitive functions were assessed by the Faolstein Mini-Mental State Examination (MMSE) scale. It evaluates orientation, memory, calculation, attention, language, and praxis, for a maximum score of 30.^{8,14,15}

Data analysis: The main outcome variable was Cognitive Function. The mean values and standard deviations (SD), or proportions of selected socio-demographic attributes were computed. Mean differences in cognitive function by hypertension status, systolic and diastolic pressure were examined using appropriate statistical test of significance. To test the independent effect of predictors on cognitive function across all stages of blood pressure, multiple linear regression analysis was done.

RESULTS:

The study includes 62 hypertensive patients that were recently diagnosed. The age range was 45 to 72 years, majority belongs to 45 to 55 years (38.7%) and the average age was 59.48 (SD 8.63). The overall mean BMI in study participant was 24.61 (SD 2.48). Other socio-demographic characteristics of study participants are shown in

Table 1.

Of the 62 hypertensive patients, 29 (46.77%) were stage 1 and 33 (53.23%) stage 2 hypertensives. Mean systolic and mean diastolic blood pressure of the study participants across various stages of blood pressure were within the range specified in the JNC VII classification of blood pressure. The mean systolic blood pressure and diastolic blood pressure for all participants was 159.16 (SD=9.19) and 98.33 (SD=6.74) (Table2)

The lowest MMSE score was 14 and the highest was 28. Overall mean score was 22.03 (SD2.10). Table 1 shows the Mean MMSE score in hypertensive persons across various socio-demographic profiles. It was observed that MMSE score was significantly decreases as the age increases ($p=0.004$). The mean MMSE score in person over 64 years of age was 21.69 (SD2.35).

The mean score of various cognitive domains is given in table 3. We studied the score of each cognitive domain separately across all stages 1 and stage 2 hypertensive patients. However, it was observed that the cognitive function score for all domains was not significantly different between stage 1 and stage 2 hypertensive patients ($p>0.05$).

The regression analysis was performed to test the independent effect of high blood pressure and age on cognition. SBP, DBP and age were included in model. Overall it was observed that the SBP, DBP and age independently shows a significant negative effect on MMSE score ($p<0.01$).

DISCUSSION:

Our study reveals a declining cognitive performance in newly detected hypertensive patients (stage 1 and stage 2 - JNC VII criteria). The cognitive function on MMSE score was not significantly different in stage 1 and stage 2 hypertensive patients. Several studies also mentioned that hypertension confer greater risk for cognitive impairment, independent of other factors.^{10, 16-18, 20, 23, 24}

The score of MMSE in hypertensive patients in our study was less across all domains. The mean

MMSE score for all participants was 26.73 (SD 3.44). Fourteen was the lowest and 28 the highest MMSE score of study participants. However this study did not include comparison group, so we cannot comment on the magnitude of the risk of declining cognitive function in hypertensive patents.

On studying the cognitive function in hypertensive patient with socio-demographic predictors, it was observed that cognitive function in recently diagnose essential hypertensive patient's decrease with increasing age. Other studies have also reported the inverse relation of age with cognitive function in hypertensive patients.^{17, 18} A multiple linear regression analysis was performed to find out the independent predictive effect of SBP, DBP and age on cognitive function in hypertensive patients ($p<0.01$). All three, systolic blood pressure, diastolic blood pressure as well as age shows a independent significant negative effect on cognition in recently diagnosed hypertensive patients. Waldstein SR¹⁰ and Brady CB et al¹⁸ also reports that in hypertensive individuals age was negatively related to performance on all of the cognitive tests in their studies.

Education does not significantly affect cognitive function in hypertensives in this study; however one study reports that a high level of education was protected against the cognitive deterioration.

With regards to score of all domains cognitive function on MMSE scale in stage 1 and stage 2 hypertensive patients, no significant difference was observed in any domain ($p>0.05$). Studies have reported that hypertension does not affect all the domains of cognitive function similarly. Cognitive functions affected by high blood pressure are related to deficits in learning, memory, attention, abstract reasoning, executive functions, visuospatial, and psychomotor abilities but were unrelated to verbal intelligence or language abilities.^{21, 29} Framingham Heart Study¹⁶ also showed varying association of various cognitive functions with hypertension. Brady CB et al¹⁸ study reports an association of hypertensive status with category fluency and immediate

recall. However this differing opinion on association of specific cognitive domain with hypertension in different studies may be due to different tools used for measuring cognitive performances. The difference in finding of our study compared to other studies may also be attributed to different inclusion criteria. Most of the other studies studied cognitive function in long duration and/or uncontrolled hypertensive patients, where our study only includes patients that were recently diagnosed; not currently taking any antihypertensive medication and without any evidence of complication or target organ damage.

The studies that we have compared were on elderly persons i.e. more than 60 years. Considering the high risk of hypertensions at relatively younger age group in south East Asian population due to higher fat deposit at lower BMI compared to their western counterpart, we also studied hypertensive patients that were relatively younger i.e. above 45 years of age. In spite of this we observed a low cognitive function in hypertensive patients across all age group; however the decrease of MMSE scores was more at higher age group.

The minimal status examination scale used in our study also has some inherent limitations because of its emphasis on language and its insensitivity towards mild deficits and is also influenced by age and education.¹⁵

Our study has some limitations; we have not studied the pathophysiologic mechanism and cause for decrease in cognitive performances in hypertensive and its clinical significance. Moreover our study does not include comparison group, we cannot comment on the magnitude of the risk of declining cognitive function in hypertensive patients.

Even though the exact mechanism of decrease cognition in hypertensive patients is not clear; several studies suggest that presence of cerebral white matter lesion (WML) is associated with impaired cognition leading to dementia and is also an important prognostic factor for the development of stroke and could be considered an early marker of brain damage.^{19, 20, 23, 24, 27-29}

Cardiovascular Heart Study²⁵ mentioned that WML and cognitive decline is associated with higher stages of blood pressure and clinical silent stroke on MRI. Mental slowing, executive deficits, memory impairment and global cognitive decline are the most common cognitive features related to WML in hypertensives.^{20, 21, 22, 26} Therefore the decreased cognitive function in hypertensives could not be considered as benign and therefore it becomes imperative to study cognitive function in all hypertensive subjects, regardless the stage and duration of blood pressure.

Conclusion

Considering this background, and our findings that both SBP and DBP apart from age are associated with reduced cognitive function, this study may have significant health implication for improving the quality of care and life of patients with essential hypertension in resource poor situations. Assessing the cognitive function would be cost effective approach to suspect early cerebral white matter changes as studies have already established the association of declining cognitive function with WML and subsequently stroke and/or dementia in hypertensive patients.

However, this was an observational cross-sectional study; therefore inferences regarding a causal relationship between essential hypertension and cognitive function could not be drawn. Similarly it is not possible to comment on the extent relative benefit of assessing cognitive function in all hypertensive patients. Therefore a more elaborate community based prospective study is needed to examine the temporal relation. Similarly an experimental study would be useful to study the value of assessing cognitive function in hypertensives on their quality of life and care in Indian setting.

Table: 1 Characteristics of the study participants

Participants characteristics		No (%)	MMSE score		
			Mean	SD	
Sex	Male	48 (77.4)	23.77	3.08	t = 1.41 P=0.68
	Female	14 (22.6)	25.00	1.79	
Age group (years)	45 – 55	24 (38.7)	25.00	1.80	ANOVA F=6.108; p=0.004
	55 – 65	22 (35.5)	26.38	2.13	
	65 – 75	16 (25.8)	24.96	2.35	
Education	Illiterate	13 (20.9)	23.44	2.90	ANOVA F=9.21; p=0.21
	Till Secondary	4 (6.5)	24.34	2.68	
	Higher sec.	7 (11.3)	24.25	0.96	
	Above	38 (61.3)	24.43	3.74	
Smoking	Never smoker	16 (25.8)	25.81	2.01	t= 1.87 p=0.68
	Ever smoker	46 (74.2)	23.44	3.13	
Alcohol	Non Alcoholic / occasional	60 (96.8)	24.16	3.56	t=0.70 p=0.29
	Regular	2 (3.2)	23.97	2.43	
BMI	18 – 24.9	20 (32.3)	24.26	3.66	t= 2.87 p=0.08
	25 – 29.9	42 (67.7)	22.44*	3.23	

Table 2: Classification of study participants as per JNC VII criteria and mean systolic and diastolic blood pressure in each category

Blood pressure -JNC VII (mm of Hg)	No (%)	Systolic Blood Pressure* Mean (SD)	Diastolic Blood Pressure# Mean (SD)
Hypertensives - Stage 1*	29 (45.77)	151.79 (SD ± 4.53)	92.62 (SD ± 1.86)
Hypertensives -Stage 2**	33 (52.23)	167.45 (SD ± 4.34)	102.27 (SD ± 6.14)
All participants***	62 (100)	159.16 (SD ± 9.19)	98.33 (SD ± 6.74)

*t= 27.57 p=0.01 ** t=18.97 p=0.01 *** t=31.23 p=0.001

Table 3: Mean (SD) MMSE score of various cognitive domain in stage 1 and stage 2 hypertensive

Cognitive domain	! Hypertensive patients (n=62)		Stage 1 Hypertensive		Stage 2 Hypertensive		t test
	Mean	SD	Mean	SD	Mean	SD	
Orientation	8.71	1.26	9.35	1.10	9.98	0.16	t=2.91 p=7.82
Registration	2.97	0.18	2.98	0.13	3.00	0.0	t=2.29 p=0.42
Attention & Calculation	2.77	1.37	3.68	1.42	4.41	0.77	t=1.01 p=0.31
Recall	1.79	0.79	2.33	0.85	2.78	0.47	t=0.13 p=0.89
Language	7.81	1.21	8.39	1.04	8.98	0.16	t=0.48 p=0.62
Total MMSE	22.03	2.10	26.73	3.44	29.15	1.33	t=0.31 p=0.75

Table 4: Multiple linear regression to find out the independent effect of SBP, DBP and Age on MMSE score in hypertensive patients

Predictor	Hypertensives patients (n=62)	
	B	SE
Systolic blood pressure	-0.386	0.021 **
Diastolic blood pressure	-0.590	0.030 **
Age	-0.136	0.023*
Constant	72.63	
R ²	0.858	

* significant at $p < 0.01$, ** significant at $p < 0.001$

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