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Assessment of Cognitive Function in Patients with Hypertension from Different Socioeconomic Statuses in India: A Two - Arm Cross-Sectional Study

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Abstract:

Objectives *- Age-related decline in cognitive functions is a common phenomenon but not uniform across all domains and varies amongst individuals. Few longitudinal studies have demonstrated the relation between elevated blood pressure and fall in cognitive function, but Indian literature in this regard is scarce. Hence, we conducted this study to determine the prevalence and occurrence of cognitive deficits in hypertensive patients, and its relation with socio-economic status.* ***Methods*** *- This was a two-arm cross-sectional study. 100 patients (hypertensives and normotensives) attending geriatric/medicine out-patient department of a tertiary care centre were recruited. Grading of hypertension was done and details of medication were taken. Presence of psychiatric/neurological complications were noted. Socio-economic status of patients was assessed using Modified Kuppuswamy's Socioeconomic Scale. Two established psychiatric evaluations namely Addenbrooke's Cognitive Examination (ACE) and Trail Making Test (TMT) were conducted.* ***Results*** *- Forgetfulness, the most common complaint, was presented by 44% cases but only by 10% controls. Amongst the hypertensives 13 patients had confusion, 2 had aggressive behaviour and 15 had behavioural changes. 94% cases had cognitive impairment in test group compared to 72% in control, by the ACE. The difference in time lag for TMT Part A between cases and controls was statistically significant ($P<0.05$). For TMT Part B, difference was not significantly different. ACE scores in hypertensives of lower socioeconomic status was significantly less ($P<0.05$).* ***Conclusion*** *- Assessment revealed significantly high prevalence of cognitive impairment in hypertensives as compared to normotensives. Early identification of cognitive dysfunction may provide considerable benefit to hypertensive patients.*

Keywords *- **Cognitive function, Hypertension, Socioeconomic status, Addenbrooke's Cognitive Examination, Trail Making Test, Kuppuswamy's Socioeconomic Scale.***

Introduction

Cognition is the processing of information by an individual. Any defect in cognition skills of an individual will lead to improper thinking, perception, memory, motivation and language.[1] Age-related decline in the cognitive functions is a common phenomenon but not uniform across all the domains and varies amongst individuals.[2] There has been an increase in the number of cases of cognitive dysfunction worldwide in recent times. A report by WHO in 2010 stated that about 7.7 million people around the world developed dementia. This ongoing spurt in the cases of dementia has led to an increase in the study of various modifiable factors leading to the disorder.[3]

Hypertension is one of the most prevalent non-communicable disease in the world and is associated with high numbers of morbidity and mortality. The World Health Organisation data on hypertension states that globally, it is accountable for about 17 million deaths per year, which is a huge one-third of all global deaths.[4-6]

Few longitudinal studies have demonstrated the relation between elevated blood pressure and a fall in cognitive function.[7] The exact mechanism behind the cognitive decline due to hypertension is not yet known, but the

knowledge in this regards is gradually increasing.[8] Cerebrovascular damage is caused by an increase in the blood pressure which is associated with increase in atherosclerosis as well as oxidative stress in the vascular wall. Damage in the subcortical white matter may be associated with transient decrease in the blood flow.[9] Hypertensive patients are associated with high risk of developing cerebral haemorrhage, both the intra-parenchymal as well as the subarachnoid type.

Indian literature in this subject is sparse. Few of the main reasons for the dearth in the Indian literature on this topic are cultural issues on performing tests for cognitive impairment, low education and high illiteracy rate.[10] In view of this lack of data available in India on the link between cognitive function and high blood pressure, it was worth taking up a study to check the correlation between cognitive deficits and hypertension in a tertiary care teaching hospital set-up in a metropolitan city of India. We conducted the study with objectives of determining the prevalence of cognitive deficits in hypertensive patients, assessing the variations in cognitive deficits in relation to hypertension, and assessing the different socio demographic factors in individuals with and without hypertension.

Materials and Methods:

The study was a pilot cross-sectional study, initiated only after obtaining permission from the Institutional Ethics Committee. Patients (hypertensives and normotensives) attending Geriatric/Medicine Outpatient Department of a tertiary care centre in Mumbai (India) constituted the study population. The patients in the OPD were screened between January 2014 to June 2015.

The inclusion criteria stated that patients of either gender aged between 50-60 years, both these years inclusive, diagnosed with hypertension as per JNC VIII criteria irrespective of their treatment status, will be considered for the study. These patients should also be able to understand, read, write and communicate in English, Marathi and Hindi and willing to give a written informed consent. Exclusion criteria were: known cognitive impairment, physical comorbidities like diabetes mellitus, endocrine disorders, other systemic illnesses, and any other condition which may interfere with evaluation, in the opinion of the investigator. Patients with co-morbid psychiatric disorders, on medications which may interfere with the cognitive function or those with visual and/or hearing impairment which may affect the outcome of psychometric tests were also excluded.

50 consecutive hypertensive patients meeting the study criteria were included in one group, while 50 consecutive normotensive patients matching for age and socio-demographic profile were included in the other group. Grading of hypertension was done and details of the medication were taken. Presence of the psychiatric/ neurological complications related to hypertension were noted. Socio-economic status of patients was assessed using Modified Kuppuswamy's Socioeconomic Status Scale. Two structured and established psychiatric evaluations namely Addenbrooke's Cognitive Examination and Trail Making Test were administered to all the patients (both cases and controls).

Addenbrooke's Cognitive Examination (ACE) is a brief cognitive test that provides evaluation of six cognitive domains (orientation, attention, memory, verbal fluency, language and visuospatial ability) and is useful for detecting dementia and mild cognitive impairment. ACE takes 15 minutes to perform, provides a MMSE score and five sub-scores that represent attention and orientation (18 points), memory (26 points), letter and category verbal fluency (14 points), language (26 points) and visuospatial ability (16 points). Total score is obtained by summing all sub-scores ranging from 0-100, out of which MMSE is a part.[11]

Trail making test (TMT) is a neuro-psychological test done mainly to measure the various domains of cognitive function of subjects like attention, speed as well as mental flexibility. There are two parts of the test, part A and part B. The two parts have different domains of testing.[12,13]

TMT Part A - Part A tests the following domain: Visual scanning, numeric sequencing, visual-motor speed. Part A requires the subject to connect 25 encircled numbers distributed on a page, by drawing lines between them.

TMT Part B - Part B tests the following cognition domains: visual-motor abilities, visual-spatial abilities, mental flexibility. Part B is similar to Part A of TMT except that the subject must alternate between numbers and letters.

The various study parameters were summarized as frequencies & percentages for categorical variables and Mean ± SD or Median (Range) for continuous variables. Unpaired t test was used to compare cases with controls in case of parametric data while Mann- Whitney U test was used for nonparametric data.

Results:

The group containing hypertensive patients was labelled as test group with the cases while the other group containing normotensive patients was called the control group, for convenience. The patients were aged between 50-60 years, the mean age of test group was 55.54 ± 3.10 years and that for the control group was 54.72 ± 3.34 years. The test group comprised of 66% males and 34% females, while the control group had 74% males and 26% females. Modified Kuppuswamy classification was used to categorize the study participants, based on the socioeconomic status. The socioeconomic status of the patients has been depicted in figure 1.

Figure 1: Socioeconomic Status of Participants

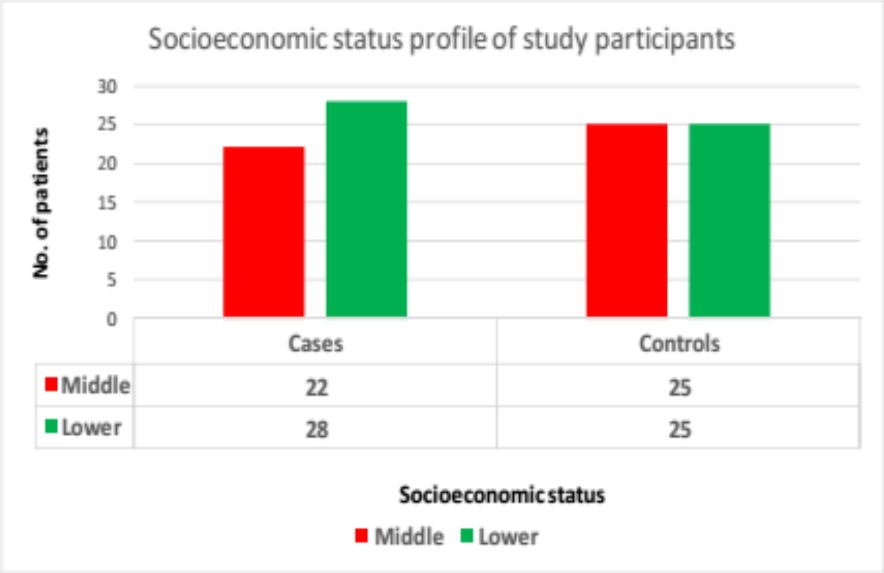


Table 1: Blood pressure in the test and control groups

Parameter assessed	Test group (mm Hg)	Control group (mm Hg)	P value
Systolic blood pressure	135.04 ± 13.71	112.64 ± 10.57	<0.0001
Diastolic blood pressure	83.76 ± 10.57	74.96 ± 7.99	<0.0001
Mean arterial blood pressure	100.86 ± 9.27	87.50 ± 8.48	<0.0001

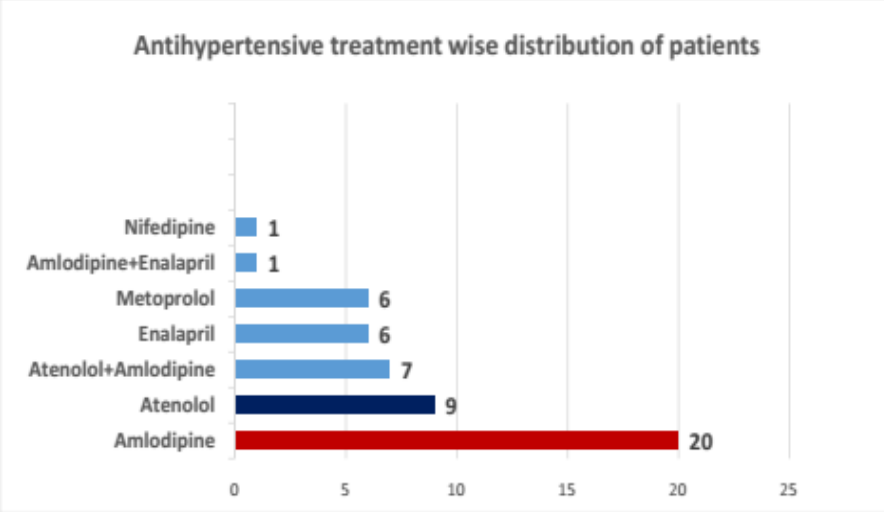
P value < 0.0001 considered statistically significant (unpaired t-test)

The mean blood pressure recording was done for all patients of both the study groups. The two groups were statistically different from each other, as depicted in table 1.

The hypertension status of the cases was assessed based on the blood pressure measurements at the time of visit. Nearly half of the patients (54%) had adequately controlled blood pressure with normal values at the time-point. However, majority (83%) of the uncontrolled cases belonged to JNC VIII Category I hypertension, only 17% patients belonged to JNC Category II. A large proportion of the patients had long standing illness with 23 patients being hypertensive for 10-15 years and 21 patients for over 15 years. 6 patients had hypertension of duration shorter than 10 years.

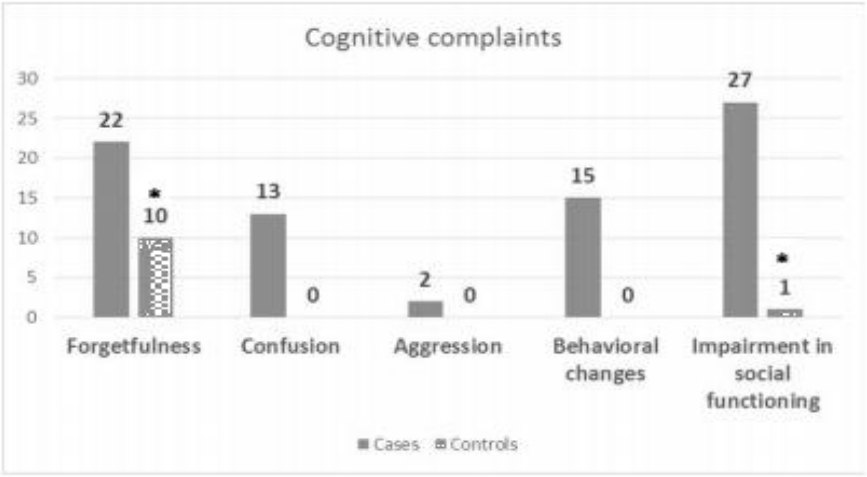
Majority of the hypertensive patients were treated with amlodipine (40%), followed by atenolol (18%). Metoprolol (12%) and enalapril (12%) were other frequently prescribed drugs. A combination of amlodipine and enalapril was prescribed in one patient, while the combination of atenolol and amlodipine was prescribed in seven patients. Figure 2 shows the pattern of anti-hypertensive prescription in our study.

Figure 2: Prescriptions of Antihypertensive drugs of patients



After obtaining clinical history, the common cognitive complaints in both the study groups were compared. Forgetfulness was the most common complaint in both the test and control group. 44% of cases in the test group presented with this complaint while only 10% of controls had forgetfulness. 13 patients in the test group had confusion, 2 reported aggressive behaviour and 15 patients had behavioural changes. These complaints have been represented in figure 3.

Figure 3: Cognitive complaints reported by study participants



*p < 0.0001 considered to be statistically highly significant (Mann Whitney U test)

Table 2: Cognitive Assessment Tests for the study groups

Test Performed	Test Group	Control Group	P Value
Addenbrooke's cognitive examination scores	61.96 ± 16.59	78.74 ± 7.8	< 0.0001*
Time taken in seconds to complete TMT Part A1	90.31 ± 29.75	77.1 ± 20.1	0.0112**
Time taken in seconds to complete TMT Part B2	206.42 ± 74.14	183.75 ± 42.25	0.0736

TMT: Trail Making Test
Values in mean + SD; 2 patients in the test group did not complete the trail test;
8 patients in test group and 2 patients in control group did not complete the trail test
**statistically significant (Mann Whitney U test); **statistically significant (Unpaired t test)*

Assessment of cognitive function was carried out by employing two designated tests, namely Addenbrooke's cognitive examination score and trail making tests. These evaluations were carried out and the parameters were compared between the cases and controls. Table 2 shows the results of these evaluations.

Prevalence of cognitive dysfunction was assessed by defining 82 as a fixed score on Addenbrooke's cognitive examination. Scores < 82 were considered as cognitive impairment. In our study, while 47 cases had scores below 82, 36 controls had similar scores. A higher prevalence (94%) was seen in test group when compared to that in control group (72%). The difference in the time lag in TMT Part A between the cases and controls was statistically significant. 2 patients in the test group did not complete the trail. However, for TMT Part B, the difference in the time lag between cases and controls was not significantly different. 8 cases and 2 controls did not complete the trail.

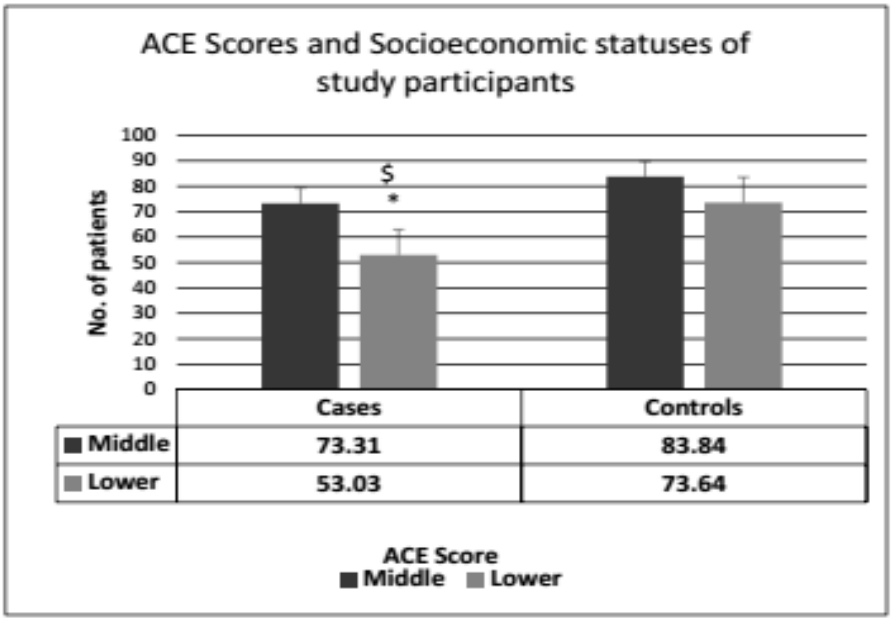
Further, scores of individual components of Addenbrooke's examination was compared between cases and controls. It was seen that the difference between test group and control group was statistically significant with all the components ($p<0.05$). The results of these components have been depicted in table 3.

Table 3: Scores of Individual Components of Addenbrooke's examination in study groups

Component	Test Group	Control Group	P Value
Composite score	61.96 ± 16.59	78.74 ± 7.8	< 0.0001*
Attention and Orientation	12.66 ± 3.77	14.94 ± 2.58	< 0.001*
Memory	14.82 ± 4.32	18.84 ± 3.45	< 0.0001*
Fluency	8.64 ± 4.82	12.06 ± 2.12	< 0.001*
Language	15.56 ± 4.76	19.14 ± 3.37	< 0.0001*
Visuospatial	10.32 ± 3.99	13.74 ± 2.33	< 0.0001*

*Values in mean + SD, *: statistically significant (Mann Whitney U test)*

Figure 4: Addenbrooke's cognitive examination scores and socioeconomic status of the study groups



ACE Score: Addenbrooke's cognitive examination score
**p < 0.001 vs. cases middle status on Kruskal Wallis ANOVA with post hoc test considered statistically significant*
$ p < 0.01 vs. control lower status on Kruskal Wallis ANOVA with post hoc test considered statistically significant

There was a statistically significant difference between the Addenbrooke's cognitive examination scores between test and control groups in the lower (test group = 53.03 ± 15.17: controls = 73.64 ± 6.19) and middle (test group = 73.31 ± 10.27: controls = 83.84 ± 3.56) socioeconomic statuses. The difference is evident in figure 4

Discussion

This study attempts to find an association between hypertension and cognitive deficits, prevalence of cognitive deficits in hypertensive patients and compare socio demographic factors in individuals with or without hypertension. Though the importance of lowering blood pressure in hypertensive subjects is well known but the relationship between hypertension and cognitive function has not been studied extensively in India. Numerous cross sectional studies investigating the relationship between blood pressure and cognition have shown conflicting relationships whilst the majority of longitudinal studies have demonstrated elevated blood pressure to be associated with cognitive decline.[14] Asian and Indian studies on the same are lacking, as we found out after a profound literature search.

The test and the control groups in our study was comparable based on age and gender. Modified Kuppuswamy classification was employed to categorize the study participants based on socioeconomic status. The socioeconomic status is an important demographic factor that may influence the onset and progression of cognitive decline. This may also have an impact on factors such as time to seek medical care and compliance to treatment. 28 of the cases and 25 of the controls belonged to lower socioeconomic status, 22 of the cases and 25 of the controls belonged to middle socioeconomic status, and it was found that patients belonging to low socioeconomic status had more cognitive impairment. The above finding is in accordance with the longitudinal cohort study conducted in Netherlands which found that low socioeconomic status is related to decline in cognitive function and this relationship is not mediated by biomedical factors i.e. heart disease, hypertension and diabetes.[15]

In our study, majority (83%) of the uncontrolled hypertensive cases belonged to JNC VIII Category I hypertension, and only 17% patients belonged to JNC Category II. There was no statistically significant difference in cognitive decline between patients belonging to JNC VIII category I and patients belonging to JNC VIII category II. Large scale studies like the Framingham study and the Honolulu-Asia aging study have shown inverse relation between hypertension and cognitive impairment.[14,16] Though the details of antihypertensive medication were captured in our study, other factors like adequacy of treatment, compliance to treatment, and impact on progression could not be assessed. We tried to tap the number of participants in test group on medication as the Syst-Eur study showed that there was reduction in the incidence of dementia in patients on treatment for hypertension.[17]

Prevalence of cognitive dysfunction was assessed by defining 82 as a fixed score on Addenbrooke's cognitive examination. Addenbrooke's scale has a high sensitivity of 99% and specificity of 100% for assessing cognitive

dysfunction. In our study, it was found that hypertensive patients had lower scores as compared to normotensive controls and difference was statistically significant. This finding is like that found in a Japanese study where hypertensives scored lower scores as compared to normotensives.[18]

Forgetfulness was the most common complaint in both the study groups, but the frequency was higher in the test group. As per a longitudinal study performed for patients of age group 46-68 years, it was found that hypertension had an adverse effect on executive or "meta" cognitive abilities, involving basic processes like attention, memory and speed of information processing.[19]

TMT was also used to assess the cognitive impairment. Though this test is not commonly used, it is considered a solid test for assessment of cognition. In a Swedish study conducted in 999 seventy-year-old men in Uppsala, cognitive function was assessed with respect to cardiovascular risk factor with the help of TMT.[20] The difference in the time lag in both Part A and B between the test and control groups was statistically significant; thus, indicating the probable relation of cognitive impairment with hypertension.

Our study was carried as a pilot project in a limited number of patients. Also, the impact of anti-hypertensive medication on progression of cognitive impairment could not be assessed in our study.

We can suggest from our study that there is a linkage with hypertension and vascular dementia that necessitates further studies to investigate whether further cognitive decline can be postponed by a more intensive preventive treatment. Early diagnosis of cognitive impairment in these patients is very important and actions to prevent further decline must be considered as early as possible before the patients develop clinical manifest dementia.

Conclusion

Our study found high prevalence of cognitive impairment in hypertensive patients as compared to normotensives, and the difference was statistically significant. Significantly lower scores on the Addenbrooke's test were seen in the hypertensive group compared to normotensive control, suggesting an early onset and a higher prevalence of cognitive impairment in hypertensive patients, when compared to the normotensive patients. Time taken by the normotensive control group population to complete both trail making test part A and part B was shorter than the time taken hypertensive cases. Thus, hypertension has clearly been shown to be a risk factor for cognitive dysfunction in individuals belonging to the age group of 50-60 years in our study. For application of results at the community level, further studies are required to assess the role of antihypertensive medications in improving cognition or their contribution in slowing down the cognitive impairment, as it remains highly controversial. Early identification of cognitive dysfunction in hypertensive patients may provide considerable benefit to patients, suggesting ways of coping with these impairments and adapting secondary preventive measures to prevent onset of dementia.

Conflict of Interest: Nil

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