Journal of Cardiovascular Disease Research

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 12, 2023

A STUDY OF COGNITIVE IMPAIRMENT IN HYPERTENSIVE PATIENTS IN A RURAL POPULATION

DR.NIDHI JAIN [1] , DR.PRASHANK AJMERA[2] , DR. APOORVA BHARGAVA [3],

DR.ANANYA BHARGAVA[4*]

[1]MBBS, MD Psychiatry, Senior Consultant, Tele MANAS Jaipur, Rajasthan, India
[2]MBBS, MD (Medicine), Senior Resident DM Cardiology, SMS Medical College, Jaipur, Rajasthan, India
[3]MDS, Conservative Dentistry and Endodontics,Consultant Endodontist,Delhi , India
[4*]MDS , Orthodontics and Dentofacial Orthopedics ,Assistant Professor (Department of Dentistry), Ruxmaniben Deepchand Gardi Medical College,Ujjain (M.P), India

Corresponding Author: Dr.Ananya Bhargava

drananyaortho@gmail.com

ABSTRACT

AIM:

1. To determine the prevalence of cognitive deficits in hypertensive patients

2. To compare cognitive deficit in patients with and without hypertension

MATERIAL AND METHODS:

A comparative cross sectional observational study including patients already diagnosed with hypertension according to JNC VIII criteria between the ages of 45 to 60 years. Cognitive function assessment was done by two tests Addenbrooke's cognitive examination score and Trail Making Test A and B.

RESULTS:

The average age was 53.57 ± 4.94 for cases and 53.04 ± 5.03 for controls. The mean Systolic Blood Pressure in cases is 136.56 ± 12.31and in controls is 114.44 ± 6.218 and mean Diastolic Blood Pressure in cases is 87.91 ± 7.29 and 72.59± 6.10 in controls. While 62 cases had scores below 82, 49 controls had similar scores. The mean time taken by the cases to complete TMT Part A was 94.27 ± 15.34 seconds while controls took lesser time of 68.00 ± 12.97 seconds and to complete TMT Part B was 207.17 ± 44.98 seconds while controls took lesser time of 163.67 ± 33.51 seconds.

CONCLUSION:

High prevalence of cognitive impairment was found in hypertensive patients as compared to normotensives. Lower scores on Addenbrooke's score were seen among the hypertensive group compared to normotensive control. Time taken by the normotensive control group to complete trail making test part A and part B was shorter than the time taken by hypertensive cases. Hypertension has been a risk factor for cognitive dysfunction in the patients in the age group of 45-60 years in our study.

KEYWORDS:

Hypertension, Cognitive Decline, Dementia, Trail Making Test

INTRODUCTION

Cognition refers to a broad range of largely invisible activities carried out by the human brain. Perceiving, thinking, knowing, reasoning, remembering, analysing, planning, paying attention, generating and synthesizing ideas, creating, judging, being aware, having insight – all these, and more, are aspects of cognition. The following is a working definition: cognition includes any and all process by which a person becomes aware of his/her situation, needs, goals, and required actions, and uses this information to implement problem solving strategies for optimal living. [1]

Cognitive decline is a part of a natural history of brain ageing. Cognitive decline may take different forms depending on the severity of the process—from physiological cognitive ageing through mild cognitive impairment (MCI), a cognitive decline greater than expected for an individual's age and education, however not affecting patients activities of daily living, till dementia, a state in which cognitive impairment is affecting activities of daily living. [2]

The normal aging process is associated with declines in certain cognitive abilities, such as processing speed and certain memory, language, visuo-spatial and executive function abilities. The age-related decline in the cognitive functions is not uniform across all the domains and varies amongst individuals. [3]

Hypertension is defined as increase in the blood pressure above the normal range. World Health Organisation defines hypertension as systolic blood pressure more than or equal to 140 mm Hg and/or diastolic blood pressure more than or equal to 90 mm Hg. It is important for the functioning of vital organs such as brain, heart and kidneys to have the blood pressure in normal range. Hypertension is among the most prevalent non-communicable diseases in the world and is a cause of high numbers of morbidity and mortality. In India, the prevalence has increased to around 31.%. The data on hypertension by World Health Organisation states that it is causing around 17 million deaths per year worldwide, also the complications of hypertension causes 9 million deaths globally each year. [3-4]

Hypertension affects the brain in many ways which has its impact on cognition. It leads to reduced cerebral blood flow and metabolism particularly in areas such as frontal and temporal lobes and subcortical areas. The changes in the vasculature associated with hypertension like arteriosclerosis, lipohyalinosis leads to white matter lesions such as infarcts, lacunae. [5]

There is moderately strong evidence to support the claim that impaired and declining speed of processing and executive function are the cognitive changes associated with chronic hypertension.[6] Many of the studies have demonstrated the effect of raised blood pressure on

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 12, 2023

cognitive impairment. This study aims to find the prevalence of cognitive deficits in patients with hypertension and to assess the variations in cognitive deficits in relation to hypertension.

MATERIAL AND METHODS

This is a cross sectional observational study that took place at Ruxmaniben Deepchand Gardi Medical College & Hospital, Ujjain including outdoor patients of both sexes attending Medicine OPD already diagnosed with hypertension according to JNC VIII criteria between the ages of 45 to 60 years. The duration of hypertension was categorized in three groups with <10 years, 10-15 years and >15 years. The control group comprised of attendant/relatives accompanying patients belonging to the same age group. Patients with known cognitive impairment, systemic illness like diabetes mellitus, endocrine disorders or any other condition which may interfere with the evaluation were excluded. Patients with schizophrenia, delusional disorders, anxiety disorders, substance use disorder excluding nicotine were also excluded. Patients with visual/hearing impairment and who didn’t give consent were also excluded. A total number of 68 cases and 68 controls were taken satisfying the criteria. The study received approval from Ethical Committee of R D Gardi Medical College, Ujjain and informed consent of all the participants were obtained.

Tools:

1. Semi structed proforma to collect socio-demographic and clinical details such as duration of hypertension, treated/untreated along with psychiatric complaints like forgetfulness, confusion, aggression, change in behavior, socio-economic functioning.
2. For Cognitive assessment Addenbrooke’s Cognitive Examination III (Hindi) and Trail Making Test were applied.
3. Addenbrooke’s Cognitive Examination III is a simple, brief, paper-and-pencil-based measure of global cognitive function. It covers five cognitive domains. Each cognitive domain measure’s specific cognitive ability, contributing to the overall score. The scale is 100 points. Each domain carries different points, as follows: 18 points are allocated to the attention and orientation domain, 26 points to the memory domain, 14 points to the verbal fluency domain, 26 points to the language domain, and 16 points to the visuospatial domain. A higher score is interpreted as better cognitive ability. [7]
4. Trail Making Test is a brief paper and pencil neuropsychological test often used for screening for cognitive impairment. Part A appears to be dependent primarily on the efficiency of visual scanning and psychomotor speed. In contrast, Part B consists of circles, some of which contain numbers and others letters. The alternation between serial sequences of letters and numbers is thought to require executive control, specifically, flexibility of thinking and greater demand for working memory. [8] If the time taken to complete Part A is less than the time taken to complete Part B, the subject is considered to have difficulties in complex conceptual tracking. In general, performance is considered impaired if scores exceed 90 seconds for part A and 270 seconds for part B. [9]

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 12, 2023

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. A p value less than 0.05 was considered to be statistically significant.

RESULTS

The average age was 53.57 ± 4.94 for cases and 53.04 ± 5.03 for controls. 64.7 % were males and 34.3% females in case group and 69.1% males and 30.9% females in the control group. The mean Systolic Blood Pressure in cases is 136.56 ± 12.31and in controls is 114.44 ± 6.218 and mean Diastolic Blood Pressure in cases is 87.91 ± 7.29 and 72.59± 6.10 in controls are statistically significant with p value <0.0001.
Majority of the patients had long standing history of hypertension with 31 cases being hypertensive for 10 – 15 years, 28 cases for more than 15 years and 9 cases had a history of less than 10 years of hypertension. Almost half of the patients (54.4%) had adequately controlled BP. In the uncontrolled group, 25% cases belonged to JNC VIII Category I hypertension, 20.6% patients belonged to JNC VIII Category II. (Table 1)

Table 1: Cognitive assessment parameters

Test	Cases	Control	P value
Addenbrooke's cognitive examination score (Mean ± SD)	62.93 ± 13.00	73.28 ± 8.05	0.000
Time taken to complete TMT A in seconds* (Mean ± SD)	94.27 ± 15.34	68.00 ± 12.97	0.000 (382)
Time taken to complete TMT B in seconds** (Mean ± SD)	207.17 ± 44.98	163.67 ± 33.51	0.000 (761)

*6 patients in the cases did not complete the trail

**15 patients from the cases group and 4 from the control group did not complete the trail

p value <0.0001 is highly significant (Mann Whitney U test)

In the Addenbrooke's cognitive examination higher scores were obtained in normotensive control group which suggests a higher prevalence of cognitive dysfunction in hypertensive patients. 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.

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 12, 2023

In our study, while 62 cases had scores below 82, 49 controls had similar scores. A higher prevalence (91%) was seen in cases when compared to 72% in controls.
Comparison of scores between different grades of hypertension was made. Scores between controlled cases (64.93 ± 10.93) and Grade I (64.7 ± 12.56) and Grade II (57.71 ± 17.59) hypertensive was not statistically significant.(Table 2)Further, scores on individual components of Addenbrooke's examination was compared between cases and controls. It was seen that the difference between cases and controls was statistically significant with all the components.

Table 2 : ACE and its component score among cases and controls

Component	**Cases** (Mean ± SD)	**Controls** (Mean ± SD)	**P value** (U Statistic)
Composite Score	62.93 ± 13.00	73.28 ± 8.05	0.000 (1174)
Attention and Orientation	13.69 ± 2.18	14.03 ± 1.82	0.551 (2177)
Memory	14.15 ± 4.51	18.15 ± 3.15	0.000 (1167)
Fluency	7.69 ± 1.94	8.69 ± 1.47	0.001 (1606)
Language	16.35 ± 3.26	20.29 ± 2.23	0.000 (689)
Visuospatial	11.03 ± 3.19	11.96 ± 1.86	0.031 (1819)

The mean time taken by the cases to complete TMT Part A was 94.27 ± 15.34 seconds while controls took lesser time of 68.00 ± 12.97 seconds. The difference in the time lag in Part A between the cases and controls was statistically highly significant. 6 patients among the cases did not complete the trail. Similarly, the mean time taken by the cases to complete TMT Part B was 207.17 ± 44.98 seconds while controls took lesser time of 163.67 ± 33.51 seconds. The difference in the time lag in Part B between cases and controls was statistically highly significant. However the time taken by controls was clearly lesser than the time taken by cases. 15 patients among the cases and 4 patients among the controls did not complete the trail.
There was a statistically significant difference between patients belonging to lower (Cases 56.46 ± 11.32; Controls 69.74 ± 5.73) and middle (Cases 72.74 ± 8.52; Controls 79.00 ± 8.04) socioeconomic statuses among cases and controls themselves as well as between cases and controls. While it may not be feasible to comment on the actual impact, the difference between the scores was striking with lower scores seen in lower socioeconomic status.

DISCUSSION

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 12, 2023

Hypertension and risk of cognitive impairment has been positively associated through various longitudinal studies. [10-12] There are myriad of pathological mechanisms proposed by which hypertension causes functional and structural changes in the brain leading to cognitive decline. [13] In this study, the mean systolic blood pressure in cases is 136.56 ± 12.31and in controls is 114.44 ± 6.218 and mean Diastolic Blood Pressure in cases is 87.91 ± 7.29 and 72.59± 6.10 in controls. Both cases and controls were statistically comparable. The gender differences were comparable and showed male preponderance in both cases and controls. Maximum patients belonged to middle and lower socio-economic strata.41 of the cases and 27 of the controls belonged to lower socioeconomic status, 42 of the cases and 26 of the controls belonged to middle socioeconomic status and the patients belonging to low socioeconomic status had more cognitive impairment. The findings described above are in accordance with the longitudinal cohort study performed in Netherlands in which 2574 men and women participated and it was found that the decline in cognition is related to low socioeconomic status and it is not mediated by factors such as heart disease, hypertension, diabetes etc. [14]

The assessment of hypertension was based on the BP measurements at the point of visit. Almost half of the patients (54.4%) had controlled BP with normal BP values at the point. In the uncontrolled cases 25% belonged to JNC VIII Category I hypertension and 20% patients belonged to JNC Category II. The difference between category I and category II was not statistically significant. The study conducted by Wilkie *et al* states that “the basis for the cognitive decline associated with aging should be considered secondary to some pathologic processes and not merely as a ‘normal’ aging process.” [15] In the longitudinal Framingham Study performed in 1956-1964, on the age group 55-80 years found an inverse relation between hypertension and cognitive impairment. [16]. The Honolulu-Asia Aging Study showed that in later life high systolic BP is a predictor of reduced cognitive function in later life. [17] Although the SPRINT trial in adults with hypertension showed that more intensive bloop pressure control (target SBP <120mmHg versus <140mmHg) did not result in significant cognitive benefit [18]

The effect of antihypertensive therapy on cognitive deficit in hypertension is controversial in previous literature and could not be commented in our study. As this was a cross – sectional study neither the adequacy and compliance to treatment or the impact on progression could be assessed. The various trials on the use of antihypertensive therapy in the elderly showed it is capable of decreasing all types of cardiovascular events. The Syst-Eur study showed that there was reduction in the incidence of dementia in patients on treatment for systolic hypertension. [19]

Prevalence of cognitive dysfunction was assessed by defining 82 as a fixed score on Addenbrooke’s cognitive examination. In our study, while 62 cases had scores below 82, only 49 controls had similar scores. A higher prevalence (91.2%) was seen in cases when compared to 72.1% in controls. A study in Japan was conducted for validation of Addenbrooke’s scale in which ACE was translated into Japanese and it was found that at a cut-off score of 82, Addenbrooke’s scale had a sensitivity of 99% and specificity of 100% and it was observed that hypertensive patients scored lower on ACE in comparison to normotensives. [20] Unlike other screening tests, the ACE-III provides the clinician with a brief multi- component cognitive profile, since it provides specific scores for different

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 12, 2023

cognitive domains: attention, memory, verbal fluency, language, and visuospatial function. [21]

Forgetfulness was the most common complaint in both cases and controls. While 44.1% of cases presented with this complaint, only 20.6% of controls had forgetfulness. 17 patients among cases had confusion, 3 had complaint of aggressive behaviour and 20 patients had behavioural changes. There were 36 cases with impairment in social functioning.
The mean scores on Addenbrooke's cognitive examination in the cases was 62.93 ± 13.00 compared to of 73.28 ± 8.05 in normotensive controls. The difference between the cases and controls was statistically highly significant. The cases and controls were compared for the 5 parameters of Addenbrooke's examination and the hypertensive patients had lower scores as compared to normotensive controls and difference was statistically significant.
In a longitudinal cohort study at National Institute on Aging Alzheimer's Disease Centres, US setting, 1,385 patients with mild cognitive impairment (MCI) and measured BP values at baseline were followed for two annual visits. Participants with MCI high BP values (SBP ≥140 mmHg or DBP ≥90 mmHg) on 2 or 3 occasions had significantly faster decline on neuropsychological measures of visuomotor sequencing, set shifting, and naming than those who were normotensive on all three occasions. [22] In the longitudinal study among the ages of 46-68 years it was found that, "High blood pressure was associated with cognitive function in middle-age in the Whitehall II", had an adverse effect on executive or "meta" cognitive abilities, implicating basic processes like attention, memory and information processing speed. [23] A Swedish study of 999 seventy-year-old men from a population based cohort study in Uppsala, followed since the age of 50 with respect to cardiovascular risk factors. At the age of 70, 24-hour ambulatory BP was monitored together with measurements of insulin sensitivity, glucose tolerance, serum lipids, and lipoproteins. Cognitive function was assessed by the MMSE and TMT. There was a strong co-relation between hypertension and cognitive decline in untreated men.[24]
In conclusion, our study suggests hypertension may contribute to cognitive decline. However, various factors like duration of illness, grade of hypertension and presence of other co-morbid illnesses affects onset, progression and degree of cognitive decline. There is a further need to investigate whether the cognitive decline can be delayed thereby preventing dire consequences like stroke, dementia affecting the quality of life and increasing the risk of mortality. It is also important to improve early detection and treatment which will have an impact in lowering the global burden of dementia.

ACKNOWLEDGEMENTS

The Authors would like to thank the study participants for their kind cooperation and support throughout the study.

CONFLICTS OF INTEREST

There were no conflicts of interest.

SOURCES OF FUNDING

None

REFERENCES

1. Soo Borson. Cognition, Aging and Disabilities: Conceptual Issues. *Phys Med Rehabil Clin N Am*. 2010 May ; 21(2): 375–382.
2. Dariusz Gąsecki & Mariusz Kwarciany & Walenty Nyka & Krzysztof Narkiewicz. Hypertension, Brain Damage and Cognitive Decline. Curr Hypertens Rep (2013) 15:547–558
3. WHO| Hypertension Available from: https://www.who.int/news-room/fact-sheets/detail/hypertension
4. Global report of hypertension: the race against a silent killer; World Health Organization. Available from: https://www.who.int/publications/i/item/9789240081062
5. Costantino Iadecola, Chair, Kristine Yaffe et al. Impact of Hypertension on Cognitive Function**.** Hypertension. 2016 December ; 68(6): e67–e94
6. Birns J, Kalra L. Cognitive function and hypertension. *Journal of Human Hypertension.* 2009; 23: 86–96.
7. Bajpai S, Upadhyay A, Sati H, Pandey RM, Chaterjee P, Dey AB. Hindi Version of Addenbrooke's Cognitive Examination III: Distinguishing Cognitive Impairment Among Older Indians at the Lower Cut-Offs. Clin Interv Aging. 2020 Mar 5;15:329-339. doi: 10.2147/CIA.S244707. PMID: 32184582; PMCID: PMC7062397.
8. Bhatia T, Shriharsh V, Adlakha S, Bisht V, Garg K, Deshpande SN. The trail making test in India. Indian J Psychiatry. 2007 Apr;49(2):113-6. doi: 10.4103/0019-5545.33258. PMID: 20711393; PMCID: PMC2917075.
9. Verma M, Tripathi M, Nehra A, Paplikar A, Varghese F, Alladi S, Narayanan J, Dhaliwal RS, Sharma M, Saroja AO, Arshad F, Divyaraj G, Ghosh A, Manae TS, Mekala S, Menon RN, Hooda R, Iyer GK, Sunitha J, Kandukuri R, Kaul S, Khan AB, Mathew R, Nandi R, Padma MV, Pauranik A, Ramakrishnan S, Sarath L, Shah U, Sylaja PN, Varma RP and Vishwanath Y (2021) Validation of ICMR Neurocognitive Toolbox for Dementia in the Linguistically Diverse Context of India. Front. Neurol. 12:661269. doi: 10.3389/fneur.2021.661269
10. Skoog I, Lernfelt B, Landahl S, Palmertz B, Andreasson LA, Nilsson L, et al. 15-year longitudinal study of blood pressure and dementia. *Lancet.* (1996) 347:1141–5. doi: 10.1016/S0140-6736(96)90608-X
11. Alpérovitch A, Blachier M, Soumaré A, Ritchie K, Dartigues JF, Richard- Harston S, et al. Blood pressure variability and risk of dementia in an elderly cohort, the Three City Study. *Alzheimers Dement.* (2014) 10:S330– 7. doi: 10.1016/j.jalz.2013.05.1777
12. Abell JG, Kivimäki M, Dugravot A, Tabak AG, Fayosse A, Shipley M, et al. Association between systolic blood pressure and dementia in the Whitehall II cohort study: role of age, duration, and threshold used to define hypertension. *Eur Heart J.* (2018) 39:3119–25. doi: 10.1093/eurheartj/ehy288

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 12, 2023

13. Canavan M and O'Donnell MJ (2022) Hypertension and Cognitive Impairment: A Review of Mechanisms and Key Concepts. Front. Neurol. 13:821135. doi: 10.3389/fneur.2022.821135
14. Koster A, Penninx BW, Bosma H, Kempen GI, Newman AB, Rubin SM, *et.al* Socioeconomic differences in cognitive decline and the role of biomedical factors SB.2005.Sep;15(8):564-71.
15. Wilkie F, Eisdorfer C. Intelligence and blood pressure in the aged. Science. 1971; 172:959–62.
16. Elias MF, Wolf PA, D'Agostino RB, Cobb J, White LR. Untreated blood pressure level is inversely related to cognitive functioning: the Framingham Study. Am J Epidemiol.1993;138:353–64.
17. Launer LJ, Masaki K, Petrovitch H, Foley D, Havlik RJ. The association between midlife blood pressure and late-life cognitive function: the Honolulu-Asia Aging Study. JAMA. 1995; 274: 1846–51.
18. SPRINT MIND Investigators for the SPRINT Research Group. et al. Effect of intensive vs standard blood pressure control on probable dementia: a randomized clinical trial. JAMA **321**, 553–561 (2019).
19. Forette I, Seux ML, Staessen JA, et al. Prevention of dementia in randomized, double-blind, placebo-controlled systolic hypertension in Europe (Syst-Eur) trial. Lancet.1998;352:1347-51.
20. Hidenori Yoshida,1,2 Seishi Terada,1 Hajime Honda,1 Yuki Kishimoto,1 Naoya Takeda,1 Etsuko Oshima,1 Keisuke Hirayama,3 Osamu Yokota1 and Yosuke Uchitomi1 Validation of the revised Addenbrooke's Cognitive Examination (ACE-R) for detecting mild cognitive impairment and dementia in a Japanese population 2011, pg10.
21. Bruno D, Schurmann Vignaga S. Addenbrooke's cognitive examination III in the diagnosis of dementia: a critical review. Neuropsychiatr Dis Treat. 2019 Feb 15;15:441-447. doi: 10.2147/NDT.S151253. PMID: 30858702; PMCID: PMC6387595.
22. Goldstein FC, Levey AI, Steenland NK. High blood pressure and cognitive decline in mild cognitive impairment. J Am Geriatr Soc. 2013 ; 61(1): 6773.
23. Singh-Manoux A1, Marmot M. High blood pressure was associated with cognitive function in middle-age in the Whitehall II study.J Clin Epidemiol. 2005 Dec;58(12):1308-15.
24. Kilander L, Nyman H, Boberg M, Hansson L, Lithell H. Hypertension Is Related to Cognitive Impairment: A 20Year Followup of 999 Men. Hypertension. 1998; 31: 780-86.