International Journal of Medical Science and Dental Research

COGNITIVE IMPAIRMENT AND MEMORY LOSS AMONG HYPERTENSIVE PATIENTS: CALL FOR EFFECTIVE PHARMACEUTICAL CARE IN PAKISTAN

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Abstract: *Hypertension is predictive of cognitive impairment. Elevated blood pressure, obesity, and high cholesterol collectively lead to complications including decline in cognitive ability. The present study was designed to explore the factors effecting cognitive impairment and memory loss among hypertensive patients in twin cities of Pakistan. A descriptive cross-sectional study design was used. A pre-validated data collection tool i.e. Mini Mental State Examination (MMSE) questionnaire, which is a practical method for grading the cognitive state of patients was distributed to a sample of 384 hypertensive patients. After data collection the data was cleaned, coded and statistically analyzed using SPSS version 21. Out of 384 respondents, 73.4% (n = 282) were males while 26.6% (n = 102) were females. About stages of disease, 45.8% (n = 176) were categorized in stage I disease while 54.2% (n = 208) were in stage II. Out of 384 hypertensive patients, 31.5% (n = 121) had normal cognition level, 53.4% (n = 204) had mild cognitive decline and 15.4% (n = 59) showed moderate cognitive decline. Significant difference ($p \geq 0.05$) among different variables such as age, gender, qualification, smoking status, occupation, stages of hypertension and income with cognitive impairment was observed. The present study concluded that majority of the hypertensive patients showed mild cognitive impairment and memory loss. Cognitive impairment and memory loss was more common among stage II hypertensive patients with CAD or diabetes. Increasing age, low education and qualification level also have negative impact on cognition and memory among hypertensive patients. Patients using beta-blockers had more cognitive decline as compared to those on other antihypertensive therapies.*

Keywords - *Cognitive impairment, memory loss, hypertension, Pakistan*

I. INTRODUCTION

Hypertension is predictive of cognitive impairment. The variables like age, gender, education, and presence of co-morbidities are the major factors associated with cognitive disability among hypertensive patients. Hypertension associated cognitive impairment increases as the age of patient increase [1].The relationship of blood pressure with cognitive function is mainly non-linear and moderated by age, gender, education and blood pressure lowering therapies. Various brain mechanisms elaborate the relationship between high blood pressure and cognitive impairment, but a complete understanding of this relationship is necessary for the preservation of cognitive functions in a hypertensive patient [2]. The exact relation between elevated blood pressure and the ability of an individual to think, remember or reason is still not well understood. High blood pressure is directly

associated with memory loss and cognitive decline. Beneficial effect of blood pressure lowering therapy on preserving cognitive ability has been reported but its mechanism is still unclear [3].

Careful monitoring and controlling or treating of both systolic and diastolic blood pressure are critical for the preservation of cognitive functioning among hypertensive patients [4]. A study reported poor performance in neurocognitive tests like delayed recall and prefrontal regional skills among hypertensive patients as compared to control group. The results of neurocognitive tests indicated the malfunctioning of cognitive ability and memory loss among hypertensive patients. Hence, these tests were found sufficiently sensitive and easy to use in clinical practice [5]. The results of another study have revealed that cognitive performance among young hypertensive patients on tests like attention/ executive functioning and memory were found significantly poor as compared to normotensive people while the difference of cognitive performance of middle age hypertensive people is not distinguished than normotensive without counting and both groups were independent of psychosocial, demographics and alcohol-related factors [6]. Elder patients having mild hypertension and slightly impaired cognitive ability have been reported at high risk for cardiovascular disease and severe cognitive decline and must be treated with antihypertensive therapy to prevent cardiovascular disabilities and further decline of cognitive function [7]. Extensive research has been conducted regarding the assessment of the relationship between hypertension and cognitive impairment with relation to different variables like age, gender, qualification etc. in developed countries. Beside this, a clear understanding of the relationship between effects of different antihypertensive therapies for prevention of cognitive ability has been established. However, to the best of our knowledge, no such research study has been ever conducted in Pakistan. Therefore, the present study was designed to explore the factors effecting cognitive impairment and memory loss among hypertensive patients in twin cities of Pakistan.

II. Methodology

A descriptive cross-sectional study design was used to explore the factors effecting cognitive impairment and memory loss among hypertensive patients in twin cities i.e. Islamabad (Federal Capital) and Rawalpindi (Twin City) of Pakistan. Study sites for this research included public and private tertiary health care facilities and hypertensive clinics located in twin cities of Pakistan. Study respondents included in the study were: any hypertensive patient (Stage I or II) with duration of disease at least one year, getting their treatment from any usual care setting (hospital, clinic, community centre), persons who were between 18-65 years old, both genders (Male vs. Female) and persons who could easily read and write were included in the study. However, hypertensive patients previously taking treatment for any other psychological disorder were excluded.

Calculation of sample size was performed by Raosoft® sample size calculator to determine the size of sample representing the study population. The calculated sample size was 384 to achieve 95% confidence interval and 5% margin of error. Convenient sampling technique was used for the study and all the respondents that were available at the time of data collection and willing to participate in the study were selected.

A pre-validated data collection tool i.e. Mini Mental State Examination (MMSE) questionnaire, which is a practical method for grading the cognitive state of patients was used. Written permission was obtained from the respective organization for using the tool. Mini Mental State Examination (MMSE) is a brief clinical test of mental status that consists of total of eleven questions. The MMSE begins with a graded assessment of orientation to place and time; this is followed by testing two aspects of memory. The first is the immediate recall for three objects presented orally, followed by a serial sevens task which is interposed to assess attention, concentration, and calculation, and also to prevent the individual from rehearsing the three objects previously learned. The final section surveys aphasia by testing functions of naming, repetition, understanding a three-stage command, reading, writing and copying a drawing. The MMSE can be easily administered by trained health care professional. The person administering the MMSE is required to be receptive about patient embarrassment if patient was unable to answer these questions. Respondents were informed that this is another way of determining how the treatment is affecting their cognitive abilities. Total score of MMSE is 30. A score range of 0-10 indicates severe cognitive impairment, 11-20 score range indicates moderate cognitive impairment, 21-25 indicates mild cognitive impairment while a score of 26-30 shows cognitive impairment of questionable significance. MMSE was self-administered by principal investigator after obtaining written/verbal consent from

the respondents. The questionnaire was collected back on the same day to avoid any study biasness. After data collection the data was cleaned, coded and statistically analyzed using SPSS version 21. Descriptive statistics comprising of frequency and percentages were calculated. Chi-Square test ($p \geq 0.05$) was used to find association among different variables.

III. Results

Out of 384 respondents, 73.4% (n = 282) were males while 26.6% (n = 102) were females. Of the total respondents, 11.5% (n = 44) were newly diagnosed cases, 37.7% (n = 118) had previous (1-2 years) clinical history of a disease and 18.2% (n = 70) had more than 10 years of duration of disease. About stages of disease, 45.8% (n = 176) were categorized in stage I disease while 54.2% (n = 208) were in stage II. Among co-morbid conditions, 36.7% (n = 114) were diabetics while 32% (n = 123) had coronary artery disease (Table 1).

Table 1 Demographics Characteristics

Indicators		**n (%)**
Age	20-30Y	32 (8.3)
	31-40Y	66 (17.2)
	41-50Y	94 (24.5)
	51-60Y	97 (25.3)
	61-75Y	95 (24.7)
Gender	Male	282 (73.4)
	Female	102 (26.6)
Marital Status	Married	345 (89.8)
	Unmarried	39 (10.2)
Level of Qualification	Secondary	100 (26.5)
	Intermediate	194 (50.5)
	Graduate	67 (17.4)
	Master	23 (6.0)
Income group	<10-20000	203(59.2)
	21,000-35000	98 (25.5)
	36,000-50,000	57 (14.8)
	>50000	26(6.8)
Duration of disease	Newly diagnosed	44 (11.5)
	1-2Y	118 (37.7)
	5-10 Y	150 (39.1)
	>10Y	70 (18.2)
Stages of disease	Stage 1	176 (45.8)
	stage 2	208 (54.2)
Class of Medication uses	ACEIs	55 (14.3)
	CCBs	61 (15.9)
	Diuretics	49 (12.8)
	Beta-blockers	74 (19.3)
	ARBs	67 (17.4)
	CCBs+ARBs	44 (11.5)
	CCBs+BB	17 (4.4)
	ACEIs+BB	17 (4.4)
Co-morbidity	Diabetes	95 (24.7)
	CAD	123 (32.0)
	CKD	14 (3.6)

	Any other	11 (2.9)
	None	141 (36.7)
Smoking Status	Yes	93(24.2)
	No	291 (75.8)
Profession	Officer	114 (29.7)
	Worker	101 (26.3)
	Retired	105 (27.3)
	Housewife	59 (15.4)
	Any other	5 (1.3)

Out of 384 respondents 31.5% (n = 121) had normal cognition level, 53.4% (n = 204) had mild cognitive decline and 15.4% (n = 59) showed moderate cognitive decline (Table 2).

Table 2. Assessment of MMSE Score among Hypertensive Patients

Indicator	Frequency n (%)
26-30 (Questionably significant)	121 (31.5)
20-25 (Mild cognition impairment)	204 (53.4)
10-19 (Moderate cognition impairment)	59 (15.4)
0-9 (Severe cognition impairment)	0 (0.0)

Out of total respondents, 11.5% (n = 44) were newly diagnosed patients. Among newly diagnosed patients, 4.4% (n = 17) had mild and 0.5% (n = 2) had moderate cognitive impairment while 39.1% (n = 150) patients had 5-10 years of disease duration and 7.3% (n = 28) of these had normal cognition, 24.2% (n = 93) had mild and 7.6% (n = 29) had a moderate cognitive impairment. Among stage I patients, 21.4% (n = 82) had mild and only 2.3% (n = 9) had moderate cognitive impairment while 31.8% (n = 122) of stage II patients had mild and 13% (n = 50) had moderate cognitive impairment (Table 3).

Table 3. Interpretation of MMSE Score according to Duration and Stages of Disease among Hypertensive Patients

Variable	Interpretation of MMSE				
Duration of disease	**Normal n (%)**	**Mild n (%)**	**Moderate n (%)**	**Total n (%)**	**P value**
Newly diagnosed	25(6.5)	17(4.4)	2(0.5)	44(11.5)	
1-2Y	56(14.6)	56(14.6)	6(1.6)	118(30.7)	
5-10 Y	28(7.3)	93(24.2)	29(7.6)	150(39.1)	**0.001**
>10Y	10(2.6)	38(9.9)	22(5.7)	70(18.2)	

Total	119(31.0)	204(53.1)	59(15.4)	382	
Stages of disease					
Stage 1	85(22.1)	82(21.4)	9(2.3)	176(45.8)	**0.001**
stage 2	36(9.4)	122(31.8)	50(13.0)	208(54.2)	

Chi-square test ($p \geq 0.05$)

Of the total respondents 14.3% (n = 55) patients were using ACEIs for the management of hypertension and among them 7.3% (n = 28) had mild and 1.6% (n = 6) had moderate cognitive impairment while among those using ARBs, 10.4% (n = 40) had mild and 3.1% (n = 12) had moderate cognitive impairment. A detailed description is given (Table 4).

Table 4. Interpretation of MMSE Score according to Class of Medication used among Hypertensive Patients

Variable	**Interpretation of MMSE**				
Class of medication uses	**Normal n (%)**	**Mild n (%)**	**Moderate n (%)**	**Total n (%)**	**P value**
ACEIs	21(5.5)	28(7.3)	6(1.6)	55(14.3)	0.36
CCBs	20(5.2)	33(8.6)	8(2.1)	61(15.9)	
Diuretics	23(6.0)	21(5.5)	5(1.3)	49(12.8)	
Beta-blockers	24(6.3)	35(9.1)	15(3.9)	74(19.3)	
ARBs	15(3.9)	40(10.4)	12(3.1)	67(17.4)	
CCBs+ARBs	6(1.6)	28(7.3)	10(2.6)	44(11.5)	
CCBs+BB	7(1.8)	10(2.6)	0(0.0)	17(4.4)	
ACEIs+BB	5(1.3)	9(2.3)	3(0.8)	17(4.4)	
Total	121(31.5)	204(53.1)	59(15.4)	384	

Chi-square test ($p \geq 0.05$)

Significant difference ($p \geq 0.05$) among different stages of hypertension and cognitive impairment was observed. Out of total respondents 24.7% (n = 95) were diabetics and 12.5% (n = 48) of them had mild and 4.9% (n = 19) had moderate cognitive impairment. Whereas, 32.0% (n = 123) had CKD and among them,

16.9% (n = 65) had mild and 6.5% (n = 25) had moderate cognitive impairment. A detailed description is given (Table no. 5).

Table 5. Interpretation of MMSE Score according to presence of Co-morbidity among Hypertensive Patients

Variable	**Interpretation of MMSE**				
Co-morbidity	**Normal n (%)**	**Mild n (%)**	**Moderate n (%)**	**Total n (%)**	**P value**
Diabetes	28(7.3)	48(12.5)	19(4.9)	95(24.7)	
CAD	33(8.6)	65(16.9)	25(6.5)	123(32.0)	
CKD	2(0.5)	11(2.9)	1(0.3)	14(3.6)	**0.003**
Any other	3(0.8)	6(1.6)	2(0.5)	11(2.9)	
None	55(14.3)	74(19.3)	12(3.1)	141(36.7)	
Total	121(31.5)	204(53.1)	59(15.4)	384	

Chi-square test ($p \geq 0.05$)

Significant difference ($p \geq 0.05$) among different variables such as age, gender, qualification, smoking status, occupation and income with cognitive impairment was observed. Of the total respondents, 17.2% (n = 66) were in 31-40 years age group and among them 7.6% (n = 29) had mild and 1% (n = 4) had moderate cognitive impairment whereas 25.3% (n = 97) of respondents were in age group of 51-60 years and among them, 18.5% (n = 71) had mild and 4.2 % (n = 16) had moderate cognitive impairment. Among males, 37.8% (n = 145) had mild and 11.7% (n = 45) had moderate cognitive impairment while among females 15.4% (n = 59) had mild and 3.6% (n = 14) had moderate cognitive impairment. A detailed description is given (Table 6).

Table 6. Interpretation of MMSE Score according to different Demographics of Hypertensive Patients

Variable	**Interpretation of MMSE**				
Age	**Normal n (%)**	**Mild n (%)**	**Moderate n (%)**	**Total n (%)**	**P value**
20-30Y	19 (8.5)	12(3.1)	1(0.3)	32(8.3)	
31-40Y	33(8.6)	29 (7.6)	4(1.0)	66(17.2)	
41-50Y	51(13.3)	38(9.9)	5(1.3)	94(24.5)	
51-60Y	10(2.6)	71(18.5)	16(4.2)	97(25.3)	**0.001**
61-75Y	8(2.1)	54(14.1)	33(8.6)	95(24.7)	
Total	121 (31.5)	204 (53.1)	59 (15.4)	384	
Gender					
Male	92(24.0)	145(37.8)	45(11.7)	282(73.4)	
Female	29(7.6)	59(15.4)	14(3.6)	102(26.6)	**0.537**
Total	121(31.5)	204(53.1)	59(15.4)	384	

Marital Status					
Married	97(25.3)	193(50.3)	55(14.3)	345(89.8)	
Unmarried	24(6.3)	11(2.9)	4(1.0)	39(10.2)	**0.001**
Total	121(31.5)	204(53.1)	59(15.4)	384	
Level of qualification					
Secondary	21(5.5)	60(15.6)	19(4.9)	100(26.0)	
Intermediate	44(11.5)	111(28.9)	39(10.2)	194(50.5)	
Graduate	37(9.6)	29(7.6)	1(0.3)	67(17.4)	**0.001**
Master	19(4.9)	4(1.0)	0(0.0)	23(6.0)	
Total	121(31.5)	204(53.1)	59(15.4)	384	
Income group					
<10-20000	33(8.6)	126(32.8)	44(11.5)	203(52.9)	
21,000-35000	43(11.2)	42(10.9)	13(3.4)	98(25.5)	
36,000-50,000	31(8.1)	26(6.8)	0(0.0)	57(14.8)	**0.001**
>50,000	14(3.6)	10(2.6)	2(0.5)	26(6.8)	
Total	121(31.5)	204(53.1)	59(15.4)	384	
Smoking Status					
Yes	39(10.2)	45(11.7)	9(2.3)	93(24.2)	
No	82(21.4)	159(41.4)	50(13.0)	291(75.8)	**0.007**
Total	121(31.5)	204(53.1)	59(15.4)	384	
Occupation					
Officer	65(16.9)	42(10.9)	7(1.8)	114(29.7)	
Worker	30(7.8)	59(15.4)	12(3.1)	101(26.3)	
Retired	9(2.3)	69(18.0)	27(7.0)	105(27.3)	**0.001**
Housewife	14(3.6)	32(8.3)	13(3.4)	59(15.4)	
Any other	3(0.8)	2(0.5)	0(0.0)	5(1.3)	
Total	121(31.5)	204(53.1)	59(15.4)	384	

Chi-square test ($p \geq 0.05$)

IV Discussion

High blood pressure or hypertension hardly has obvious symptoms but if untreated it increases the risk of serious complications like heart attack and strokes [8]. The current study showed an association between different stages of hypertension and cognitive ability. Stage II hypertensive patients had moderate cognitive impairment. Similar findings that baseline blood pressure SBP> 160mmHg was related to a 14% increased risk of cognitive decline over the 9 years of follow up was reported [9]. Hypertension and diabetes mellitus are positively associated with cognitive decline even in a middle-aged group, however, interventions or treatment of these disorder before the age of 60 become prolific to preserve cognitive ability or functioning in a patient [10]. The results of the present study are in line with these findings and reported significant impact of diabetes and CAD on cognitive impairment of hypertensive patients. Extensive research has been conducted to identify the drug of choice to preserve cognitive ability in hypertensive patients [11]. The present study reported that anti-hypertensive medications influence the cognitive ability of hypertensive patients. Higher percentage of cognitive impairment was observed among hypertensive patients on beta-blockers, whereas low cognitive impairment was observed in patients using diuretics. Moreover, patients on calcium channel blockers/ARB combination and on ACEI monotherapy showed comparatively less cognitive impairment than patients on beta-blocker monotherapy. Similar findings of ACE inhibitors and calcium channel blockers were proven more effective in delaying cognative decline than beta blockers and diuretics [12]. Cognitive decline or impairment is positively correlated with high blood pressure particularly in a middle-aged group but this association decreases with increasing age [13]. The results of the present study showed that hypertensive elderly patients above 60 years of age had relatively more cognitive impairment. Similar findings from another study reported association of hypertension with poor cognitive functioning, specifically in patients of age 70 years or above [14]. Adults with higher literacy rate had better cognition than those with lower literacy rate (Wight et al., 2006). The current study showed that hypertensive patients with low education level had moderate level of cognitive impairment. Moreover, the present study also revealed an association between occupation/employment status and cognitive ability of hypertensive patients. It was observed that hypertensive patients who were employed at better designations had better cognitive ability than those who were un-employed. Similar results of less cognitive decline among highly educated women placed at better professional positions was reported as compared to less educated women and housewives of same age [15]. Furthermore, the present study showed significant association among income level and cognitive impairment. Low income was related to more cognitive decline among hypertensive patients. Similar results were reported by a study conducted in America identifying low socioeconomic status responsible for cognitive impairment in elderly patients (Koster et al., 2005).

V. Conclusion

The present study concluded that majority of the hypertensive patients showed mild cognitive impairment and memory loss. Cognitive impairment and memory loss was more common among stage II hypertensive patients with CAD or diabetes. Increasing age, low education and qualification level also have negative impact on cognition and memory among hypertensive patients. Patients using beta-blockers had more cognitive decline as compared to those on other antihypertensive therapies. Therefore, sscreening procedures for cognitive impairment among hypertensive patients must be devised to identify patients at increased risk of accelerated cognitive decline at an early disease stage for development of effective individualized treatment regimen. Moreover, longitudinal studies must be conducted to explore the factors associated with cognitive decline and memory loss in hypertension. Furthermore, the impact of poor blood pressure control and medication non adherence on psychomotor functions among hypertensive patients must be further explored.

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