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Research Article

PREVALENCE AND PATTERN OF COGNITIVE IMPAIRMENT IN PATIENTS ON MAINTENANCE HEMODIALYSIS

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ABSTRACT

Background: Cognitive impairment is defined as a deficit in at least two aspects of cognitive function. The important aspects of cognition are attention, memory, language, visuo-spatial skills, and frontal/executive functions. Different pattern of cognitive impairment are seen in patients with CKD not on hemodialysis and those on hemodialysis. This study was conducted to know the prevalence and pattern of cognitive impairment in patients on chronic hemodialysis. **Methods:** This was a cross sectional study and was conducted at hemodialysis unit of Shifa International Hospitals, Islamabad. The study was performed over a period of six months and 250 hemodialysis patients were recruited through consecutive non probability sampling technique and were looked for cognitive impairment by using minimental state examination questionnaire translated in Urdu. **Results:** Out of 250 patients, mean age was 49 $\pm$ 8.4 years. 92 (37%) were females and 158 (63%) were male patients. Education level of 133 (53%) patients were up to secondary school, 99 (40%) patients were higher secondary and 18 (7%) patients were masters. 43(17%) of patients were on hemodialysis for 4-6 months, 95(38%) of patients for 7-12 months, 78(31%) of patients for 13-24 months and 34(13%) of patients for> 24 months. The minimum MMSE score of patients were minimum of 26 and maximum of 30 with mean score of 28.5$\pm$0.811. Out of 250, 230(92%) patients had cognitive impairment. Mean scores in different MMSE domains like for orientation score was 9.5$\pm$0.497, for registration 2.9 $\pm$0.289, attention and calculation score was 4.738+ 0.5000, recall score was 2.8$\pm$0.352, language score was 8.5 $\pm$0.538. **Conclusion:** The study concluded that patients on hemodialysis have cognitive impairment and there is no relation of cognitive impairment with duration and frequency of hemodialysis, age , gender, level of education of patients. P value was insignificant.

KEY WORDS

Chronic Renal Failure, Hemodialysis, Cognitive Impairment

1 | INTRODUCTION

Cognitive impairment is defined as a deficit in at least two aspects of cognitive function[1]. The important aspects of cognition are attention, memory, language, visuo-spatial skills, and frontal/executive functions[2]. Cognitive impairment is said to be mild, when person can perform its daily activities while dementia affects activities of daily living and behavior[1].Cognitive impairment and dementia are commonly seen in patients with advanced chronic

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kidney disease (CKD) but are poorly recognized by nephrologists[3]. Different pattern of cognitive impairment are seen in patients with CKD not on hemodialysis and those on hemodialysis. A recent study found that patients on dialysis performed more poorly than the general population on tasks assessing executive function[4] and had low scores in logical reasoning, verbal learning, motor skills, verbal fluency, visuo-spatial memory tests[5]. A study was done recently in CKD patients, observed different mean scores in different tasks assessing orientation (4.5 ± 0.8), registration (3 ±0.3), attention and calculation (2.8 ± 0.6), recall (4.5 ±1.3),language(3.9 ±0.4), praxis (5.3 ±1.3)[6].Neuropsychological performance and short-term memory improves with maintenance hemodialysis despite the possible persistence of other cognitive dysfunctions in the domains of attention, cognitive flexibility, memory, and learning.[7] The prevalence of cognitive impairment in chronic hemodialysis (HD) patients is almost 30–80% [8]. Several factors may help to explain the association between CKD and cognitive decline and these are either vascular risk factors like hypertension, diabetes mellitus, hypercholesterolemia, cigarette smoking and cardiovascular disease, hyperhomocysteinemia, hemostatic abnormalities , inflammation, and oxidative stress or nonvascular risk factors like anemia, use of multiple medications, Sleep disturbances resulting in an impaired concentration, excessive daytime fatigue and possibly cognitive dysfunction, secondary hyperparathyroidism leading to an increased calcium uptake impairs metabolism of neurotransmitters such as brain gamma-aminobutyric acid, norepinephrine and acetylcholine, uremic toxins such as guanidine compounds. (creatinine , guanidine etc) also have a neurotoxic effect by activation of *N*-methyl-D-aspartate receptors[9].

Cognitive functions can be assessed by MMSE[1]. It is a cognitive tool which can assess and monitor the cognitive function of patients including orientation, memory, language, attention, calculation and to follow simple verbal and written commands over time[10].Recently, studies showed that the MMSE is able to detect progression of cognitive impairment in HD patients as well[11]. MMSE is also translated and validated in Urdu recently[9]. The interpretation of MMSE should take into account the level of education, language, psychiatric illness, level of functioning, sensory impairment[12].In this study we have found out the frequency and different pattern of cognitive impairment in hemodialysis patients and on the basis of results we can devise future management plans.

2 | MATERIAL AND METHODS

The study was cross sectional study and was conducted at hemodialysis unit of Shifa international hospitals, Islamabad. The study was done over a period of six months and sample was selected on the basis of consecutive non probability sampling technique and only those were selected who fulfill inclusion criteria. Inclusion criteria was (i)all adult males and females aged between 18-60 years (ii)On hemodialysis for at least greater than 3 months i.e only adults and chronic hemodialysis patients were selected. Exclusion criteria was any patient with the history of stroke, psychiatric problems, visual and auditory problems, chronic liver disease and post renal transplant and now again on dialysis were excluded because they can either cause dementia or can result in difficulty in understanding given commands.

The study was started after taking approval from ethical committee of hospital. A written informed consent was taken prior to data collection. Detailed history regarding age, sex, social status, frequency of hemodialysis, past history were recorded by the principal investigator. Cognitive impairment was assessed by using validated mini mental score examination translated in Urdu. Questionnaire has 5 different parts and each part has its own scoring written on the right side of that part. Patients were given different commands to perform and each correct answer has a score of one. In this way total score in each part was noted in the Performa. Patient scores in different parts were added and total score of less than 30(which is normal) was considered as cognitive impairment. Similarly scores of less than normal in any part were also be considered as having deficit in that aspect of cognition. Data was collected as shown in proforma (Appendix 1)

All collected data was entered in SPSS version 21.0. Quantitative variables like age, MMSE score and MMSE domains score were presented as mean ± SD, and qualitative variables like sex and cognitive impairment were presented as proportions (%). Effect modifiers like age, gender, duration and frequency of hemodialysis, history of kidney transplant andlevel of education were controlled by stratification. Post stratification chi square test was applied. P-value of less than or equal to 0.05 was considered significant.

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3 | RESULTS

Out of 250 patients, the minimum and maximum age of patients were 24 years and 68 years respectively with the mean age of 49 years with STD of± 8.4 years. (Table No. 01) Out of 250 patients, 92 (37%) were female and 158 (63%) were male. Results are presented in the pie graph below. (Chart No. 01). Out of 250 patients, the education level of 133 (53%)patients were up to secondary school, 99 (40%) patients were higher secondary and 18 (7%) patients did masters. (Table No. 02). Similarly regarding duration of time on hemodialysis,43(17%) of patients were on dialysis for 4-6 months, 95(38%) for 7-12 months, 78(31%) for 13-24 months and 34(13%) for> 24 months. (Table No. 03) No patient has a history of renal transplant before. (Table No. 04)

Regarding frequency of dialysis, 07 (2.8%) patients were on dialysis 1 session/week. 217 (86.8%) on 2 session/week and 26 (10.4%) on 3 session/week. (Table No. 05) The minimum MMSE score of patients was 26 and maximum was 30 and a mean score of 28.5 with STD of ±0.811. The minimum orientation score was 9, maximum score was 10 and a mean score of 9.51 with STD of ±0.497. (Table No. 06) The minimum registration score was 2, maximum score was 3 and a mean score of 2.9 with STD of ±0.289. The minimum attention and calculation score was 3, maximum score was 5 and a mean score was 4.74 with STD of ±0.50. The minimum recall score was 2, maximum score was 3 and a mean score was 2.8 with STD of ±0.352. The minimum language score was 7, maximum score was 9 and a mean score was 8.5 with STD of ±0.538. (Table No. 07). Out of 250 patients, cognitive impairment was present in 230(92%) patients. (Table No. 08) Out of 230 with cognitive impairment, 150 were males 92 were females. P-value was insignificant. (Table No. 09) Depending upon the level of education and cognitive impairment,121 out of 133 patients who were educated upto secondary school,93 out of 99 who were educated upto higher secondary school and 16 out of 18 who were educated upto masters level showed cognitive impairment. P-Value was insignificant. (Table No. 10)

Regarding duration of dialysis and cognitive impairment, patients whose dialysis duration were 4-6 months, 36 showed cognitive impairment, with 7-12 months duration, 87 showed cognitive impairment, with 13-24 months duration,76 showed cognitive impairment and with those on hemodialysis for >24 months ,31 showed cognitive impairment. P-Value was insignificant. (Table No. 11) Similarly regarding frequency of dialysis, In patients in which frequency of dialysis was 1 /week 06 showed cognitive impairment, 02 /week; 198 showed cognitive impairment and those with 03 /week ,26 had cognitive impairment. P-Value was insignificant. (Table No. 13) In patients with age category of 18-29 years; 11 had cognitive impairment, in 30-39 years category; 16 had cognitive impairment, in 40-49 years category;81 showed cognitive impairment, in age category 50-59 years ;112 patients showed cognitive impairment while in 60-69 years category; 10 had cognitive impairment. P-Value was insignificant. (Table No. 14)

Table 1 Descriptive Statistics of Age (N=250)

Variable	Minimum	Maximum	Mean	Std. Deviation
Age of Patients	24	68	49.34	8.379

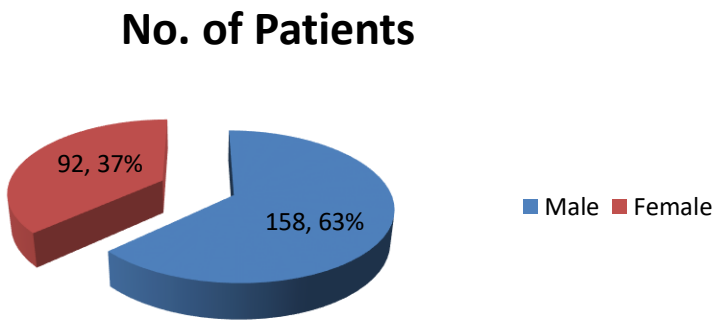

Figure 1: Frequency distribution of gender

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Table 2 Frequency Statistics of Level of Education (N = 250)

Level of Education	Frequency	Percent
Upto Secondary School	133	53.2
Higher Secondary School	99	39.6
Masters	18	7.2
Total	250	100.0

Table 3 Frequency Statistics of Duration of Dialysis (N = 250)

Duration of Dialysis	Frequency	Percent
4-6 months	43	17.2
7-12 months	95	38.0
13-24 months	78	31.2
> 24 months	34	13.6
Total	250	100.0

Table 4 Frequency Statistics of History of Renal Transplant (N = 250)

History of Renal Transplant	Frequency	Percent
No	250	100.0
Yes	0	0

Table 5 Frequency Statistics of Cycles of Dialysis/week N = 250

Cycle of Dialysis	Frequency	Percent
1 cycle/week	07	2.8
2 cycles/week	217	86.8
3 cycles/week	26	10.4
Total	250	100.0

Table 6 Descriptive Statistics of MMSE Score of patients (N = 250)

MMSE Score of Patients	Minimum	Maximum	Mean	Std. Deviation
MMSE Score of Patients	26.00	30.00	28.5000	0.8113254

Table 7 Descriptive Statistics of MMSE Domain Score of patients (N = 250)

MMSE Domain Score of Patients	Minimum	Maximum	Mean	Std. Deviation
Orientation score	9.00	10.00	9.508	0.497
Registration Score	2.00	3.00	2.9080	0.28961
Attention and Calculation Score	3.00	5.00	4.738	0.5000
Recall Score	2.00	3.00	2.8560	0.35179
Language Score	7.00	9.00	8.4560	0.53779

Table 8 Frequency Statistics of Presence of Cognitive Impairment (N = 250)

Presence of Cognitive Impairment	Frequency	Percent
Yes	230	92.0
No	20	8.0
Total	250	100.0

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Table 9 Post Stratification presence of Cognitive Impairment on basis of Gender (N = 250)

Presence of Cognitive Impairment on basis of Gender		Presence of Cognitive Impairment		P-Value
		Yes	No	
Gender of Patients	Male	148	10	
	Female	82	10	0.202
Total		230	20	

Table 10 Post Stratification presence of Cognitive Impairment on basis of Level of Education (N = 250)

presence of Cognitive Impairment on basis of Level of Education		Presence of Cognitive Impairment		P-Value
		Yes	No	
Level of Education	Upto Secondary School	121	12	
	Higher Secondary School	93	6	
	Masters	16	2	0.628
Total		230	20	

Table 11 Post Stratification presence of Cognitive Impairment on basis of Duration of Dialysis (N=250)

Presence of Cognitive Impairment on basis of Duration of Dialysis		Presence of Cognitive Impairment		
		Yes	No	P-Value
Duration of Dialysis (months)	4-6 months	36	7	
	7-12 months	87	8	
	13-24 months	76	2	0.066
	> 24 months	31	3	
Total		230	20	

Table 12 Post Stratification presence of Cognitive Impairment on basis of History of Renal Transplant (N = 250)

Presence of Cognitive Impairment on basis of History of Renal Transplant		Presence of Cognitive Impairment		P-Value
		Yes	No	
History of renal transplant	No	230	20	
Total		230	20	-

Table 13 Post Stratification presence of Cognitive Impairment on basis of Frequency of Dialysis (N = 250)

Presence of Cognitive Impairment on basis of Frequency of Dialysis		Presence of Cognitive Impairment		
		Yes	No	P-Value
Frequency of Dialysis	1 cycle/week	06	01	
	2 cycles/week	198	19	
	3 cycles/week	26	0	0.246
Total		230	20	

Table 14 Post Stratification presence of Cognitive Impairment on basis of Age Category (N = 250)

Presence of Cognitive Impairment on basis of Age Category		Presence of Cognitive Impairment		
		Yes	No	P-Value
Category of Age	18-29 years	11	01	
	30-39 years	16	01	
	40-49 years	81	07	
	50-59 years	112	10	
	60-69 years	10	01	0.998
Total		230	20	

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4 | DISCUSSION

The existing study has shown relationship with cognitive impairment, and chronic renal failure on hemodialysis. Analysis of results revealed that there was moderate and severe cognitive impairment found among 70% hemodialysis patients. Those patients belong to age group of fifty five years and above. Chronic cognitive impairment is not diagnosed yet. Past studies have revealed high graded association between cognitive function in CKD patients and glomercular filtration rate. There is a possibility that conventional hemodialysis procedure can induce recurrent episodes of severe cerebral ischemia. This might cause acute decline in cognitive function during dialysis process[13]. Comparative study was conducted having eighty sample size and findings revealed that 80 subjects at stage III and IV with CKD do not require dialysis but subjects at stage five require hemodialysis. The mean score for their age was calculated as M= 62.5, S.D=14.3. The researchers have used CVLT, 3MS and Trails B tests. There was graded association found among CKD and cognitive function. The mean values for CVLT, Trails B and 3MS were insignificant for subjects with ESRD on the contrary for subjects with CKD it was ($p<0001$). Findings on CVLT immediate were ($p=0.01$); Trails B ($p<0.001$); and delayed ($p<0.001$) were worst for those subjects with CKD but does not require dialysis for published norms. Likewise, with decreasing kidney function the fraction of patients with impairment on Trail B and 3MS were increased[14].

Another study was conducted. The nature of the study was cross-sectional. Numbers of participants were 3679. This study was based on dementia in the community of Ebersberg (INVADE) composed the community based cohort study and intervention project on cerebrovascular diseases. In that study 10.8% patients had cognitive impairment i.e. 396. Mild to moderate and severe kidney disease at baseline were 9.9, 5.8 and 21.5% across groups with normal renal function[15]. A new factor for cognitive impairment and dementia is emerged which is chronic kidney disease. Yet findings of the studies are not consistent and yet to be verified. Researchers have conducted systematic review of literature as well as longitudinal and cross-sectional studies to investigate the relationship between CKD and cognitive impairment. Most of the studies confirmed the relationship. Majority of the studies reported the relationship between two variables studied. Among 54779 participants reported a relationship of cognitive decline in CKD patients as compared to non CKD patients (OR 1.65, 95% CI 1.32–2.05; $p < 0.001$, and OR 1.39, 95% CI 1.15–1.68; $p < 0.001$, respectively).[16]Using a cross-sectional design, the authors measured cognitive function in 374 hemodialysis patients aged 55 years and older. Of 338 subjects who completed testing in at least two of the three cognitive domains, 13.9% (95% CI 10.4, 18.1) were classified with mild impairment, 36.1% (31.0, 41.5) with moderate impairment, 37.3% (32.1, 42.7) with severe impairment, and 12.7% (9.4, 16.8) with normal cognition. Only 2.9% had a documented history of cognitive impairment. Factors associated with severe cognitive impairment on adjusted logistic regression were stroke (adjusted OR [AOR] 1.95; 95% CI 1.08, 3.49; $p< 0.03$), equilibrated Kt/V > 1.2 (1.67; 1.01, 2.75; $p< 0.05$), and education >12 years (0.32; 0.14, 0.72; $p< 0.01$). The AOR for severe cognitive impairment in a random sample of 101 hemodialysis patients vs an age-matched comparison group was 3.54 (1.28, 9.78; $p< 0.02$).[17]

5 | CONCLUSION

This study showed that most of the patients on hemodialysis have cognitive impairment and there is no relation of cognitive impairment with duration and frequency of hemodialysis, age, gender and level of education of patients.

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