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Physiology

COMPARISON OF COGNITIVE FUNCTIONS BETWEEN DIABETIC CHRONIC KIDNEY DISEASE AND NON DIABETIC CHRONIC KIDNEY DISEASE PATIENTS (STAGE 5D)

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ABSTRACT

Background: In recent years there is a change in the clinical scenario all over the world with NCD in rising trend compared to the communicable diseases. Chronic Kidney Disease (CKD) is becoming more prevalent in developing countries like India because of increase in the number of persons getting affected by diabetes and hypertension. Cognitive dysfunction is an alarming new complication in them affecting their quality of living.

Methods: After getting informed consent, cognitive function of 30 diabetic CKD and 30 non diabetic CKD and age and sex matched controls was assessed by NIMHANS Neuropsychology battery 2004 and comparison between these 3 groups by one way annova and Post Hoc Turkey HSD tests

Results: Cognitive function scores of diabetic CKD patients were less than non diabetic CKD patients which in turn was less than their age and sex matched controls. These results were statistically significant with P value less than 0.001

Conclusion: In this study it is found out that diabetes contributes more to the cognitive deterioration in CKD patients. Early identification and correcting these factors may improve the cognitive function, which inturn causes improvement in quality of living as well as life expectancy of CKD patient

KEYWORDS : Cognitive dysfunction, Chronic Kidney Disease (CKD), Diabetes.

INTRODUCTION

Cognitive decline has become a major deteriorating health problem in old aged people creating difficulties to take vital decisions, to carry out their daily activities and making them totally dependent on other family members. The affected individuals lose their self-confidence, isolate themselves and do not stick onto the treatment regimen which finally leads onto major compromise in their quality of life as well as life span. Its prevalence in older generations living in South India was estimated to be around 11.5 %[1]. Recently diabetes, hypertension and chronic kidney disease (CKD) were found to be the independent risk factors for cognitive deterioration due to more oxidative stress and altered function of vessel wall endothelium[2]. Nearly 80 % of CKD patients were affected with cognitive deterioration and this impairment advances as the disease progresses in its severity[3].

MATERIALS AND METHODS

After getting ethical clearance, a case control study was conducted in the department of Physiology, in association with department of Nephrology in Coimbatore Medical College and Hospital, Coimbatore. After getting written consent 30 diabetic CKD and 30 non diabetic CKD patients of both gender with age group between 18 and 60 years, with eGFR less than 15 ml /min /1.73 m2, for more than 3 months of duration were included in this study. Age, gender, BMI and education matched normal individuals were used as controls. Cognition was assessed by **NIMHANS Neuropsychology Battery 2004.**

It includes various tests for different cognitive domains namely

- Motor Speed - Finger Tapping Tests
- Mental Speed - Digital Symbol Substitution Test
- Focussed Attention - Color Trails 1 and 2
- Sustained Attention - Digital Vigilance Test
- Divided Attention - Triad Test
- Phonemic Fluency - Controlled Oral Word Association Test
- Visual Fluency - Design Fluency Test
- Verbal and Visual Working Memory - Verbal and Visual Back Test 1 and 2
- Internally guided Verbal and Visual memory - Self Ordered Pointing Tests
- Planning - Tower of London Tests
- Response Inhibition - Stroop Test
- Verbal Comprehension - Token Test
- Verbal Learning - Rey's Auditory Learning Tests
- Logical Memory - Passage recall test
- Visuo Spatial Memory - Complex figure test
- Visual Learning & Memory - Complex Figure Recall and Design Learning Test

Two types of scores one based on number of correct responses and other based on time taken to complete the test was given. Cognitive function was compared between diabetic CKD, non diabetic CKD and their controls.

RESULTS:

Statistical Significance of the difference which exist between three groups was Assessed using One Way Anova and the significance of the difference within the groups was tested by Post Hoc Turkey test. 'p' value < 0.05 is considered to be statistically significant.

Mean age in diabetic CKD group, non diabetic CKD and control group is 44.6, 44.9 and 43.3 years respectively and there is no significant difference in age between these three groups. Equal number of male and female were included in all 3 groups.

Table 1: Comparison of Cognitive tests between 3 Groups (One way Anova)

Cognitive test	Diabetic CKD	Non diabetic CKD	Control	P value
Motor speed Right hand taps	25.80 ± 2.683	32.67 ± 3.021	53.23 ± 3.501	.000
Motor speed Left hand taps	23.70 ± 2.466	30.43 ± 2.812	50.43 ± 3.266	.000
Mental Speed (Time)	591.13 ± 112.052	498.97 ± 88.839	172.77 ± 27.575	.000
Color Trail 1 (Time)	196.27 ± 34.580	142.67 ± 15.493	44.80 ± 12.455	.000
Color Trail 2 (Time)	515.97 ±102.931	346.97 ± 46.464	95.90 ± 18.391	.000
Digital Vigilance (Time)	1082.57 ± 101.125	924.03 ± 92.040	354.27 ± 44.265	.000
Digital Vigilance Error	8.00 ± 1.462	3.63 ± 1.629	0.13 ± 0.346	.000
Divided attention Error	14.27 ± 2.504	9.53 ± 1.042	0.47 ± 0.681	.000
Verbal fluency	2.13 ± 0.819	3.37 ± 0.999	11.10 ± 2.155	.000
Category fluency	4.47 ± 1.008	7.70 ± 1.022	15.90 ± 2.171	.000

Design – Free	3.77 ± 1.104	4.10 ± 1.125	16.40 ± 4.223	.000
Design – Fixed	1.47 ± 1.042	1.73 ± 0.868	11.57 ± 2.269	.000
Verbal 1 back Hit	5.00 ± 1.050	6.93 ± 0.828	9.00 ± 0.000	.000
Verbal 1 back Error	7.60 ± 2.111	3.67 ± 1.213	0.00 ± 0.000	.000
Verbal 2 back Hit	3.03 ± 0.928	4.27 .907	8.67 ± 0.661	.000
Verbal 2 back Error	12.73 ± 2.545	7.03 ± 2.042	0.47 ± 0.860	.000
Visual 1 back Hit	5.77 ± 1.006	7.07 ± 0.944	8.9 ± 0.355	.000
Visual 1 back Error	4.10 ± 1.125	3.00 ± 1.232	0.13 ± 0.434	.000
Visual 2 back Hit	2.20 ± 0.805	4.33 ± 1.093	8.63 ± 0.718	.000
Visual 2 back Error	9.10 ± 1.729	5.23 ± 1.251	0.47 ± 0.937	.000
SOPT – Word Error	5.40 ± 0.894	3.80 ± 0.761	0.37 ± 0.615	.000
SOPT – Picture Error	5.03 ± 0.765	3.97 ± 0.890	0.17 ± 0.379	.000
Tower Of London - Minimum Moves	2.57 ± 1.223	5.13 ± 0.776	11.50 ± 1.075	.000
Response Inhibition	407.7 ± 93.785	265.80 ± 35.161	83.90 ± 18.773	.000
Token Test	22.17 ± 3.435	27.43 ± 2.012	35.67 ± 0.711	.000
AVLT - LTPR	34.53 ± 9.540	65.10 ± 8.323	93.57 ± 6.735	.000
Passage - Immediate Recall	4.83 ± 1.416	6.33 ± 1.348	19.07 ± 2.273	.000
Passage – Delyed Recall	2.90 ± 1.373	4.97 ± 1.629	18.00 ± 2.792	.000
Visuo Spatial Memory	27.92 ± 30.68	28.95 ± 31.11	31.50 ± 3.869	.000
Figure - Immediate Recall	8.70 ± 4.928	10.93 ± 2.753	31.93 ± 4.258	.000
Figure – Delayed Recall	5.10 ± 3.968	7.23 ± 2.542	28.37 ± 3.819	.000
Design - Delayed Recall	3.10 ± 1.989	8.30 ± 1.950	44.03 ± 7.757	.000

Table 2: Post Hoc Test - Tukey HSD:

Tests	Difference between the groups		P value
Motor Speed, Mental speed, Color Trails 1 and 2, Digital Vigilance Time and Errors, Divided Attention Errors, Verbal and Category Fluency, Verbal N Back Hits and Errors, Visual N Back Hits and Errors, SOPT word and Picture Errors, Tower Of London, Response Inhibition, Token Test, AVLT – LTPR, Passage – Immediate and Delayed Memory, Visuo Spatial Learning and memory, Design Delayed Recall	Diabetic CKD	Non Diabetic CKD Control	0.000
	Non Diabetic CKD	Diabetic CKD Control	0.000
	Control	Diabetic CKD Non Diabetic CKD	0.000

Significant difference exist between 1) Diabetic CKD and Non diabetic CKD, 2) Non diabetic CKD and Controls and 3) Controls and Diabetic CKD.

Table 3: Pos Hoc Test - Turkey - HSD

Tests	Difference Between The Groups		P Value
Design Free	Diabetic CKD	Non Diabetic CKD Control	0.873 0.000
	Non Diabetic CKD	Diabetic CKD Control	0.873 0.000
	Control	Diabetic CKD Non Diabetic CKD	0.000
Design Fixed	Diabetic CKD	Non Diabetic CKD Control	0.778 0.000
	Non Diabetic CKD	Diabetic CKD Control	0.778 0.000
	Control	Diabetic CKD Non Diabetic CKD	0.000

In design Fluency alone there is no significant difference between diabetic and non diabetic CKD. But there is significant difference exist between: Diabetic CKD and controls As well as between Non diabetic CKD and controls

Discussion:

In the current study which was conducted in 30 diabetic CKD, 30 non diabetic CKD and their age and sex matched controls using NIMHANS Neuropsychology Battery 2004, it was found out there was statistically significant deterioration of cognitive functions in CKD patients compared to their controls in almost all cognitive domains including Motor Speed, Mental Speed, Attention (Focused, Sustained and Divided Attention), Executive Functions (Phonemic Fluency, Category Fluency, Visual Fluency, Verbal and Visual Working memory, Planning, Response Inhibition, Verbal comprehension, Learning and Memory (Verbal, Logical, Visuo Spatial, Visual).

In the current study, CKD patients were subdivided into two groups namely diabetic CKD and non diabetic CKD and the difference between them related to cognitive function was assessed. It was found out that cognitive function scores of diabetic CKD patients were less than non diabetic CKD patients. The time taken to complete the task and number of errors committed by diabetic CKD were more than non diabetic CKD patients which were inturn more than the controls and these differences were again found out to be statistically significant with P value less than 0.001.

Most common etiology of CKD is diabetes. In recent studies it is found to be an independent risk factor for cognitive dysfunction as it affects the endothelial function of cerebral vasculature [3,4,5]. Atrophy of hippocampus and amygdala were noticed in Type 2 diabetics. Hippocampus plays a vital function in memory and it has numerous receptors for the hormone Insulin to act over. As a result there occurs memory disturbances in diabetic patients[6]. Changes in the White Matter of Brain seen in diabetic patients affects cognitive domains like mental speed, motor speed, attention, execution and memory[7]. In addition to it, hyperglycemia leads to excessive cellular oxidative phosphorylation mechanism causing accumulation of glutamate, which in excess is lethal to neurons[8].

Hailpern SM, Melamed ML, Cohen HL and Hostetter TH similar to the current study found out there was deficit in visual attention and learning in Stages 1 to 3 CKD patients and explained this on the same grounds of traditional endothelial risks including age, diabetes, hypertension, dyslipidemia[9].

Elias MF, et al studies concluded that in CKD patients there was a deficit in visuo - spatial skills, immediate and delayed recall memory, planning, attention in CKD patients due to micro vascular risk factors, oxidative stress and white matter lesions. In their study, however there was no statistically significant deficit in Verbal memory and working memory in CKD patients[10]. Etgen T, Chonchol M, Förstl H, Sander D similarly confirmed an independent relationship between renal disease and decline in cognition and proposed the same traditional endothelial risk factors as reason behind cognitive deficit[11]

CONCLUSION:

The current study implies that cognitive deterioration was statistically significant in CKD patients compared to their age and sex matched controls. In sub-group analysis there was significantly more cognitive deterioration present in diabetic CKD than non diabetic CKD patients. Various vascular as well as neurodegenerative factors contribute to the

rapid deterioration of cognitive functions in CKD patients. In this study it is found out that diabetes contributes more to the cognitive deterioration in CKD patients. Early identification and correcting these factors may improve the cognitive function, which inturn causes improvement in quality of living as well as life expectancy of CKD patient

FUTURE SCOPE OF THE STUDY

As an extension of this study pharmacological trials can be employed by giving medicines to control diabetes in CKD patients(Stage5D) and repeating the cognitive assessment tests to find out the level of improvement in various cognitive domains.

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