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Correlation of Urine D-Ribose with MMSE Scores of Patients with Alzheimer's Disease as Compared to Normal Participants

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ABSTRACT

Background And Objective: Type 1 diabetes mellitus (T1DM) is a D-glucose metabolic disorder characterized by autoimmune destruction of pancreatic β-cells, leading to insulin deficiency and hyperglycaemia. Therefore, the main objective of the study is to find the correlation of urine D-ribose with MMSE scores of patients with Alzheimer's disease as compared to normal participants. **Material And Methods:** This descriptive study was conducted in University of Lahore Teaching Hospital during January 2016 to December 2019. Participants were enrolled by dementia specialists in the research team. The diagnosis of AD was based on a detailed medical history, comprehensive physical examination, neuropsychological assessments, relevant blood test, and brain imaging examination (CT or MRI, and PET when necessary) and according to NINCDS-ADRDA criteria. **Results:** The data was collected from 100 participants, 50 in each group. Comparison of urine D-ribose concentrations between AD patients and cognitively normal participants resulted significantly in difference ($P < 0.05$). Since the relation between endogenous formaldehyde and cognitive impairment has been found, we measured the formaldehyde concentration in urine as positive control. An extremely significant ($P < 0.0001$) difference of the formaldehyde concentration was observed between AD patients and cognitively normal participants. **Conclusion:** It is concluded that D-ribose levels of AD patients were significantly elevated compared with those of age-matched cognitively normal control.

INTRODUCTION

Type 1 diabetes mellitus (T1DM) is a D-glucose metabolic disorder characterized by autoimmune destruction of pancreatic β-cells, leading to insulin deficiency and hyperglycaemia. T1DM can affect different organs and result in many complications; among these complications, diabetic encephalopathy is diabetes-induced brain damage[1]. As early as 1922, diabetes was recognized to lead to cognitive dysfunction. Because an increasing number of people are diagnosed with T1DM or type 2 diabetes mellitus (T2DM), diabetic encephalopathy has become widely recognized. Patients with diabetic encephalopathy show both mental and physical symptoms, including an altered mental state, cognitive decline, memory lapses, and changes in personality[2]. Compared with people without diabetes mellitus, people with diabetes are at higher risk of cognitive decline and dementia, such as Alzheimer's disease.

D-ribose, which is naturally found in human body, participates in numerous biochemical processes, especially in energy production[3]. D-ribose is much more reactive with protein than D-glucose such as glycation of neuronal Tau and α-synuclein under the same experimental conditions, acting as one of the major contributors to the Glycation of Serum Protein (GSP) and Hemoglobin (HbA1c). Intraperitoneal injection of D-ribose leads to elevation of formaldehyde levels in mouse brain[4]. Ribosylated Tau protein forms globular aggregation that is cytotoxic to neuronal cells. Excess and long-term administration of D-ribose induces cognitive impairment followed by amyloid-β deposition and Tau hyperphosphorylation in mouse hippocampus and cortex[5].

Weight loss is also a major clinical feature of Alzheimer’s disease (AD). According to Purdy, acceleration in the rate of weight loss is a harbinger of the change from a non-demented status to Alzheimer’s-type dementia. Weight loss primarily results from chronic dehydration, which may be one of the preventable risk factors for Alzheimer’s disease. Chronic dehydration is regarded as a common symptom of patients with age-related cognitive impairment, particularly those with AD[6]. Alzheimer’s disease is characterized by a tendency to exhibit malnutrition, which is present even in the mild-moderate stages, and a tendency to exhibit dehydration that appears in the severe stage. Hyperosmotic stress induces apoptosis and Tau phosphorylation in human neuroblastoma cells. Greater weight loss is associated with increased disease severity and mortality[7].

Therefore, the main objective of the study is to find the correlation of urine D-ribose with MMSE scores of patients with Alzheimer's disease as compared to normal participants.

MATERIAL AND METHODS

This descriptive study was conducted in University of Lahore Teaching Hospital during January 2016 to December 2019. Participants were enrolled by dementia specialists in the research team. The diagnosis of AD was based on a detailed medical history, comprehensive physical examination, neuropsychological assessments, relevant blood test, and brain imaging examination (CT or MRI, and PET when necessary) and according to NINCDS-ADRDA criteria.

Inclusion criteria

- Age > 55 years
- Confirmed patients of AD

Exclusion criteria

- All patients having hyperglycemia, with life threatening disease, with severe mental illness were excluded from this study.

Data collection

All the data were collected through a questionnaire. The MMSE is a 30-point questionnaire which is used to measure cognitive impairments. It examines functions of attention, calculation, recall, language, ability to follow simple commands and orientation. A 1.0 ml urine sample was centrifuged at 12,000 rpm for 30 min. A 0.4 ml of the supernatant was mixed with 0.6 ml 4-(3-methyl-5-oxo-2-pyrazolin-1-yl) benzoic acid in 50% methanol. Samples were centrifuged and then reacted in a 70° C water bath for 90 min; this was followed by centrifugation. Urine D-ribose were measured through enzymatic kit method. Then we compare these values with the normal participants.

The data was collected and analysed using SPSS version 17. All values were expressed in ean and standard deviation.

RESULTS

The data was collected from 100 participants, 50 in each group. Comparison of urine D-ribose concentrations between AD patients and cognitively normal participants resulted significantly in difference ($P < 0.05$). Since the relation between endogenous formaldehyde and cognitive impairment has been found, we measured the formaldehyde concentration in urine as positive control. An extremely significant ($P < 0.0001$) difference of the formaldehyde concentration was observed between AD patients and cognitively normal participants. There are different variations in urine D-ribose levels in patients with AD of different genders. Significant ($P < 0.05$) difference was obtained between female patients and female controls.

Table No. 1: Demographic data of participants**.**

	Total	**Normal**	**AD**	***P***
Age				
≤60	11	10	1	<0.05
61-74	43	27	16	<0.05
≥75	39	7	32	<0.05
MMSE (score)				
≤5	28	0	28	<0.05
6-10	13	0	13	<0.05
11-20	7	0	7	<0.05
21--24	1	0	1	<0.05
25-30	44	44	0	<0.05
CDR				
0	44	44	0	<0.05
1	9	0	9	<0.05
2	11	0	11	<0.05
3	29	0	29	<0.05

Table No. 2: Analysis between urine D-ribose or formaldehyde and cognitive scores.

Participants	Age (year ± SD)	Between rib and CS		Between FA and CS	
		*R	*P* values	*R	*P* values
Total (n = 100)	73.1 ± 9.6	-0.3169	0.0012	-0.4212	0.0000
Normal (n = 50)	66.8 ± 6.7	-0.3215	0.0333	-0.1208	0.4348
Female (n = 59)	73.8 ± 10.3	-0.3471	0.0071	-0.4252	0.0008
Male (n = 37)	72.1 ± 8.5	-0.3182	0.0667	-0.4659	0.0055

DISCUSSION

T1DM results in long-term complications in the central nervous system, causing brain cellular dysfunction and cognitive deficits. As reported in a recent study, T2DM patients suffer from D-ribose and D-glucose dys-metabolism[8]. We have noticed that the correlation between D-ribose levels and cognitive abilities is more likely to occur in female participants. D-ribose levels of female AD patients were notably higher than that of cognitively normal participants. However, significant differences were not observed in male AD patients. According to Schmidt and colleagues, there are sex differences in AD[9]. First, the prevalence of AD is higher in women than in men. Second, women have a broader spectrum of dementia related behavioural symptoms with a predominance of depression, while aggression is more frequent in men than in women[10-12]. Third, gender differences were also showed in expression of anti-oxidative enzymes and post-menopausal hormonal changes. Finally, as described by Mathys and colleagues, an overrepresentation of female cells in AD-associated subpopulations, and substantially different transcriptional responses between sexes in multiple cell types, including oligo dendrocytes[13]. Thus, the significant elevation of D-ribose levels also suggests the difference in the metabolism of D-ribose in female AD patients. Whether endogenous D-ribose could be selectively used for women with AD needs further clarifying[14-16].

CONCLUSION

It is concluded that D-ribose levels of AD patients were significantly elevated compared with those of age-matched cognitively normal control. AD patient's suffered from high levels of urine D-ribose, especially in female AD patients.

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