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Relationship between Serum Lipid Levels and the Size of Hippocampus

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A B S T R A C T

Today, cognitive disorder is one of the considered issues and many people all over the world are suffering from Alzheimer's disease and other cognitive disorders and dementia. Studies have shown a reduction in the size of the hippocampus in Alzheimer's disease and have suggested that it can be used to evaluate Alzheimer's disease and its progression. The purpose of this study was to investigate the relationship between serum lipids levels and the size of the hippocampus. In an analytical-descriptive study, 41 patients with different clinical symptoms whom referred to take brain magnetic resonance image (MRI) in a center under the direction of Tabriz University of Medical Sciences (Tabriz, Iran) were evaluated. Right and left hippocampal and brain volume was calculated by MRI at coronal T1-weighted. In these patients level of serum low-density lipoprotein (LDL), high-density lipoprotein (HDL), triglycerides (TG), and total cholesterol were measured. The mean age of patients was 54.09±3.11 years. 21 patients (51.22%) were male and 20 patients (48.78%) were female. HDL cholesterol level in patients was 51.55±10.23 mg/dl. Mean LDL-C levels in patients was 123.63±47.42 mg/dl. The average volume of the left hippocampus was 1.62±0.39 ml and the average volume of the right hippocampus was 1.61±0.42 ml. There was no significant correlation between serum lipid profile levels with the size of the hippocampus ($p>0.05$). In present study, there was a weak positive correlation between serum level of HDL-C, TG with right and left hippocampal to brain volume ratio, but the correlation was not statistically significant, and there was a weak negative correlation between serum total cholesterol with right and left hippocampal to brain volume ratio, but the correlation is not statistically significant too.

Introduction

Today, about 36 million people all over the world are suffering from Alzheimer's disease and other cognitive disorders and dementia (1). Alzheimer's disease is a neuro-degenerative disorder of unknown origin that causes dementia (2). Studies have suggested that prevalence and incidence of Alzheimer's disease and other dementia

disease are increasing and age of dementia's onset is declining (3, 4). Cognitive impairment like Alzheimer's disease can cause death, and also before death, cause of disability and reduced quality of life and has a high morbidity (5). High blood pressure, high plasma cholesterol level, diabetes, and diet-related disorders such as obesity, also were shown to be associated with Alzheimer's disease (6, 7). Cholesterol is essential substance for the structure and function of neurons and also has important role in metabolism pathway of β-amyloid, therefore some studies suggested that it may have also a pathogenic role in Alzheimer disease and other dementia disease (8, 9). Epidemiological studies reported the association of dyslipidemia and risk of cardiovascular disease with dementia disease such as Alzheimer (10, 11).

Studies have shown a reduction in the size of the hippocampus in Alzheimer's disease and have suggested that it can be used to evaluate Alzheimer's disease and its progression (12). Pathology of Alzheimer's disease includes degeneration of neurons and atrophy of the hippocampus, so Alzheimer's disease also known as hippocampal dementia (13).

Some studies suggested that hyperlipidemia alongside other risk factors, such as hypertension, smoking, and diabetes mellitus, can increase the incidence of dementia (14, 15). Finally, proving the correlation between serum lipid levels and hippocampus size could have prognostic effect in dementia disease and may reduce its costs. The aim of present study was to investigate the relationship between serum lipids levels and the size of the hippocampus.

Materials and Methods

During present descriptive analytical study which was performed from February 2013 to February 2015, patients with different clinical symptoms of cognitive impairment whom referred to take brain Magnetic resonance image (MRI) in Radiology main clinic of Tabriz University of Medical Science (Tabriz, Iran) (which is an imaging center under the direction of Tabriz University of Medical Sciences) were evaluated.

Inclusion criteria were, age 50 to 60 years and lack of pathology in brain imaging with MRI. Exclusion criteria were, having chronic diseases such as diabetes, hypertension, cancer and post-traumatic stress disorder (PTSD) (with respect to the likely impacts on the size of the hippocampus in several studies), use of lipid-lowering drugs, Family history of Alzheimer's disease is a form of "behavioral and cognitive disorders in first-degree relatives of older than 60 years with no history of trauma", smoker patients, and chronic alcohol consumes. After considering inclusion and exclusion criteria and explaining the purpose of the study to patients, and getting informed consent, finally, 41 patients were included to study.

Brain MRI images were obtained using 1.5 Tesla Siemens power. Imaging protocol included images of axial, coronal and sagittal sequences T1-weighted ([TR / TE] 552/12) and sequence T2-weighted ([TR / TE] 4000/120) - which had been set on the device as default settings.

Patient's demographic information and past medical histories were collected. Right and left hippocampal and brain volume was calculated by MRI at coronal T1-weighted. Overall brain size was determined as a confounding factor. Level of serum low-density lipoprotein (LDL), high-density lipoprotein (HDL), triglycerides (TG), and total cholesterol were measured in main

laboratory of Tabriz University of Medical Science (Tabriz, Iran) (which is a referral in the North West of Iran).

The study protocol was approved by Ethics Committee of Tabriz University of Medical Science which was followed Helsinki declaration.

Collected information has been presented as mean±standard deviation (mean±SD) and also as frequency and percentage. Statistical analysis was performed by SPSS software package version 16.0 for windows (SPSS Inc., Chicago, USA). The Pearson correlation coefficient (r) was calculated. To compare quantitative variables Student T-test was used. In all cases of study, results were statistically considered as significant with $P \leq 0.05$.

Results and Discussion

The mean age of patients was 54.09±3.11 years. Male to female ratio was 1.05:1 and 21 patients (51.22%) were male and 20 patients (48.78%) were female. There were no chronic disease, malignant, and PTSD in any patients. HDL cholesterol in patients was 51.55±10.23 mg/dl, LDL cholesterol level was 123.63±47.42 mg/dl, TG level was 186.68±99.99 mg/dl, and total cholesterol was 216.97±57.30 mg/dl.

The average volume of the left hippocampus was 1.62±0.39 ml and the average volume of the right hippocampus was 1.61±0.42 ml. The average size of patients' brains was 1185.90±137.85 ml. According to overall size of the brain as a confounding variable, the ratio of the left and right hippocampus to the brain size was calculated separately. The average ratio of left hippocampus volume to brain volume was 0.0014±0.00032 and the average ratio of right hippocampus volume to brain volume was 0.0014±0.00034.

There was no significant difference between male and female in the size of right hippocampus volume (P=0.111) and left hippocampus volume (P=0.080). There was no significant correlation between patient's age with the size of right hippocampus volume (P=0.165) and left hippocampus volume (P=0.068) and brain volume (P=0.330).

The correlation between serum lipid levels with the size of right and left hippocampus volume and their ratio to brain volume are according to table1.

There was a slight positive correlation between HDL & TG levels and ratio of right and Left hippocampus volume to brain volume, but this correlation was not statistically significant ($p>0.05$), and also there was a slight positive correlation between LDL and ratio of right hippocampus volume to brain volume, but this correlation was not statistically significant too ($p>0.05$).

There was a slight negative correlation between total cholesterol levels and ratio of right and Left hippocampus volume to brain volume, but this correlation was not statistically significant ($p>0.05$), and also there was a slight negative correlation between LDL and ratio of left hippocampus volume to brain volume, but this correlation was not statistically significant too ($p>0.05$).

In the general case, there was no significant correlation between serum lipid profile levels with the size of the hippocampus ($p>0.05$).

Changes in the temporal lobe, is a highly sensitive marker for Alzheimer's disease and almost all patients have at least a moderate degree of atrophy of the hippocampus with dilatation temporal horn. Neuroimaging

studies have focused on the assessment of temporal lobe in Alzheimer's disease, and suggested to exam pathological changes of Alzheimer's, by computerized tomography (CT) scan or MRI (16).

In present study, we investigated the relationship between serum lipids levels with the size of the hippocampus. According this study, there was no significant correlation between serum lipid profile levels with the size of the hippocampus ($p>0.05$). In a study on 85 patients with cognitive disorder, there was a significant correlation between HDL level with hippocampus size and HDL had a protective effect on hippocampus atrophy, but there was no significant correlation between serum LDL and total cholesterol with hippocampus size (17). Another study showed that HDL was as an independent factor from Apo-lipoprotein E that had a direct correlate with the gray matter of the temporal lobes, and patients who had lower levels of HDL, had severe cognitive impairment (18), also in present study there was positive correlation between serum HDL level and hippocampus volume, but this is not statistically significant (right hippocampus volume: P=0.621 and left hippocampus volume: P=0.598). As our study, some studies do not show a significant correlation between serum lipids and brain damage (17), further studies with larger sample sizes is indicated.

A study on rabbits showed that high levels of dietary total cholesterol increase in deposition of amyloid in the hippocampus, which can lead to disease exacerbation in Alzheimer's disease (19). Also our study showed a negative correlation between total cholesterol levels and hippocampus volume, but it was no statistically significant (right hippocampus volume: P=0.776 and left hippocampus volume: P=0.630). Also a study suggested that, cholesterol depletion may reduce the accumulation of beta peptide amyloid in hippocampal neurons (20).

Table.1

Table1. correlation between serum lipid levels with the size of right and left hippocampus volume and their ratio to brain volume

	HDL		LDL		TG		total cholesterol	
	r	p-value	r	p-value	r	p-value	r	p-value
right hippocampus	-0.80	0.621	-0.46	0.776	0.002	0.988	-0.046	0.776
left hippocampus	-0.85	0.598	-0.78	0.630	0.036	0.821	0.078	0.630
ratio of right hippocampus volume to brain volume	0.061	0.703	0.032	0.844	0.006	0.970	-0.010	0.948
ratio of Left hippocampus volume to brain volume	0.077	0.632	-0.063	0.694	0.017	0.918	-0.051	0.750

Eventually in our study, there was a positive correlation between HDL & TG levels and hippocampus volume, and there was a negative correlation between total cholesterol levels and hippocampus volume, but they were not statistically significant. In

a prospective study on HDL, TG, and total cholesterol on memory, only low levels of LDL was correlate with memory weakness (21). In this regard, some studies suggest that controlling of the plasma lipid level may not only improve quality of dementia disease control but could also potentially affect the rate of disease progression (22).

Controversial findings in this area are due to the complexity of the relationship between serum lipids and the size of the hippocampus. This type of studies indicating the clinical significance of serum levels of lipids, to prevent the development and progression of Alzheimer's disease and other cognitive disorders. We propose that to do these types of studies in a greater sample of population.

In conclusion, based on results of this study, some lipid profile levels such as HDL and TG may have positive correlation with hippocampus size and some lipid profiles such as total cholesterol level may has negative correlation with hippocampus size and LDL level may has a dual effect on hippocampus size. To achieve more definitive results, conducting similar studies with consideration of other interfering factors such as hormonal factors are necessary.

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