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Original Article:

Evaluation of Lipid Profile, Apo B/ Apo A Ratio and Lpa and its Relationship with Cognitive Disorders in the Older Adults: Birjand Longitudinal Aging Study

Sara Hamdamian[1,2], Asghar Zarban[3], Mitra Moodi[4], Farshad Sharifi[5], Rasoul Raesi[6,7], Mohammad Dehghani Firoozabadi[8*]

1. Social Determinants of Health Research Center, Birjand University of Medical Sciences, Birjand, Iran.
2. Birjand University of Medical Sciences, Birjand, Iran.
3. Department of Clinical Biochemistry, School of Medicine, Cardiovascular Diseases Research Center, Birjand University of Medical Sciences, Birjand, Iran.
4. Department of Health Promotion and Education, School of Health, Social Determinants of Health Research Center, Birjand University of Medical Sciences, Birjand, Iran.
5. Elderly Health Research Center, Endocrinology and Metabolism Population Sciences Institute, Tehran University of Medical Sciences, Tehran, Iran.
6. Department of Health Services Management, Mashhad University of Medical Sciences, Mashhad, Iran.
7. Department of Nursing, Torbat Jam Faculty of Medical Sciences, Torbat Jam, Iran.
8. Department of Neurology, School of Medicine, Cardiovascular Diseases Research Center, Birjand University of Medical Sciences, Birjand, Iran.

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*** Corresponding author:**

Mohammad Dehghani Firoozabadi, MD.

Address: Department of Neurology, School of Medicine, Cardiovascular Diseases Research Center, Birjand University of Medical Sciences, Birjand, Iran.

E-mail:
mdehghani44@yahoo.com

Abstract

Introduction: Accurate and timely diagnosis of mild cognitive disorders is essential to prevent their progression to dementia. This study aimed to determine the relationship among the serum levels of lipid markers of cognitive disorders in older adults in Birjand.

Materials and Methods: The community-based cohort study was performed on 1400 older adults population (60 years and older) living in urban and rural areas of Birjand, among whom 242 older adults were selected by multi-stage random sampling; the Mini-Mental State Examination Cognitive Disorders Questionnaire was completed, and five cc of blood samples were taken to assess Triglyceride, Cholesterol, Low density lipoprotein, High-density lipoprotein, lipoprotein a, Apo lipoprotein A, and Apo lipoprotein B.

Results: The mean age of participants was 70.6± 6.96 years. 55.4% were women. The level of MMSE was significantly different based on the demographic information. Mean serum levels of Lipid profile, Apo B/ Apo A Ratio, and LP a, were not significantly different from MMSE.

Conclusion: The study showed a significant relationship between demographic information and MMSE level, so it can be used to improve the cognitive level of older adults by changing their life situation, marital status, and education. However, the parameters of Lipid profile, Apo B/ Apo A Ratio, and LP a are not used to diagnose cognitive disorders in older adults.

Keywords: Apo B/ Apo A Ratio, Apo A, Apo B, Cognitive disorders, Lipid profile, Lpa.

1. Introduction

In recent decades, advances in health care have lowered mortality and improved community life expectancy. The world's older adult population is estimated to be over 900 million [1], and this is 7.5 percent for Iran, according to the most recent census, and in the not-too-distant future, 40 percent of Iran's population will be comprised of the elderly [2]. As people get older, their physiological and psychological abilities gradually decrease. As a result, they become prone to cognitive disorders [3, 4], which affect the quality of life of the individuals; this has a significant financial burden for the health care system and patients [4].

Cognitive disorders are divided into mild cognitive disorders, dementia or significant cognitive disorders, and acute or delirium [5]. Diagnosis is often based on clinical examinations and neuropsychological tests. Patient history, CT imaging, MRI, and cognitive tests such as MMSE can be helpful in the diagnostic processes. Accurate and simple identification of cognitive problems, on the other hand, has become a source of difficulty in recent years. In order to prevent minor cognitive impairments from progressing to dementia, it is crucial to make a precise and early diagnosis [6, 7].Various studies have identified several factors in the development or progression of cognitive impairment, including genetic factors (mutations in genes encoding amyloid precursor proteins), chronic diseases, metabolic syndrome, dietary status, serum folate, and metals levels [7, 8]. Other studies have reported an association among the serum lipids such as LDL, Apo B, and cognitive impairment [9, 10]. One study found that elevated cholesterol and LDL increased the risk of cognitive impairment in Chinese older adults [11-13].

It is vital to find a plasma biomarker involved in developing cognitive disorders and making an accurate diagnosis of the disease [3, 9, 14, 15]. We chose the numerous lipid variables connected with genetic and environmental factors in this research informed by the rising trend of aging, the increase in the frequency of cognitive impairments, and the findings of many studies on the genetic and environmental causes of cognitive deficiencies. This study investigates the relationship among the serum levels of lipid markers and cognitive disorders in the older adults in Birjand.

2. Materials and Methods

Study population

This cross-sectional analysis drew upon the data of the Birjand Cohort Study a large population-based study designed to assess mental health and related risk factors in the elderly. Baseline information was gathered from 1400 older adults (60 years and older) living in urban and rural areas of Birjand, among whom 242 subjects were selected by multi-stage random sampling [16]. Participants whose ages were equal to or more than 60 and who have granted their informed consent entered the study. Exclusion criteria were set as follows: older adults death, older adults with severe cerebral stroke, history of brain surgery, mental retardation, Subdural hematoma, brain tumor, brain abscess, a systemic disorder known as the cause of dementia such as chronic liver or kidney disease, hypothyroidism, hypercalcemia, systemic infection, Vitamin B_{12} deficiency, implantation of a brain shunt and history of normal-pressure hydrocephalus, and patients with vision and hearing problems.

Eligible people were included in the research on the initial visit after a review of their medical records and adherence to the inclusion and exclusion criteria. Participants (or Care-givers) were asked to fill out a demographic questionnaire, containing data on age, gender, marital status, education level, and life situation (loneliness/ living with family).

After obtaining informed consent from all participants, the objectives of the study were explained. The ethics committee of Birjand University of Medical Sciences approved the present study protocol (IR.BUMS.REC.1399.296).

Cognitive function

Mini-Mental State Examination (MMSE) was used to assess cognitive function and impairment. A trained neurology resident prepared the patient to fully participate, prevented the patient's reaction of embarrassment and anger and familiarized him/her with the procedure. MMSE test is a 30-point scale evaluating orientation to time and place (10 points), short-term and episodic long-term memory (6 points), attention and concentration (5 points), language naming, writing items (8 points), and visual function (1 point). A total score greater than 25 (25 -30) was considered normal, and values below that ($\leq$ 24) were regarded as cognitive disorders [17, 18]. This brief mental evaluation test is used for rapid screening in cognitive impairment. This test can be accomplished in about 10 minutes which is usually carried out in the clinician's office [2, 19, 20].

Blood sampling

Five cc of blood sample were taken from each participant after over-night fasting (10 to 12 hours)

from the brachial vein by a laboratory expert according to the hospital's standard method. After blood clotting, the serum samples were isolated (in a centrifuge at 3000 rpm for 10 minutes). The serum samples were then stored in a freezer a -80 °C until the parameters were evaluated.

Measurement of lipid profile items was fulfilled by Enzymatic colorimetric methods, and serum concentration of Apolipoprotein-A (apo-A), Apolipoprotein-B (apo-B), and Lipoprotein-a (Lp-a) were measured by Immunoturbidometric method (Pars Azmoon, Tehran, Iran). Fasting serum Triglyceride (TG), Total cholesterol (Chol), High-density lipoprotein (HDL), and low-density lipoprotein (LDL) were evaluated using the enzymatic method (Bionic, Iran).

Statistical analysis

SPSS software, version 16 (SPSS Inc, Texas, US), was used to analyze the data. Kolmogorov-Smirnov test was applied to evaluate the normality of the data. Values were expressed as mean and standard deviation (SD), median and inter-quartile range (IQR), or relative frequency. Categorical values were compared among the groups using the chi-square test. Independent T-test or Mann-Whitney tests were performed to analyze continuous parameters in case of normal or non-normal distribution, respectively. Logistic regression analysis was conducted to obtain odds ratio (OR) and 95% confidence interval (95% CI); variables with p-value<0.2 based on univariate logistic regression entered the multivariate logistic regression model.P values <0.05 were considered as significant.

3. Results

The mean age of the older adults was 70.6 ±6.96 years. From among the 242 older adults, 134 were female (55.4%) and 108 were male (44.6%). Most of the older adults were married (81.8%). 105 patients (43.4%) had normal MMSE. The elderly was divided into three groups in terms of age including 60 to 70, 70 to 80, and more than 80 years. Other pieces of information about the patients are presented in Table 1.

As shown in Table 2, age, gender, marital status, level of education, and life situation of the older adults were significantly different (P< 0.05), although serum level of lipid profile parameters, Apo B/ Apo A Ratio and Lp a level according to MMSE in older adults was not significantly different (P> 0.05).

Table 1. Demographic information and clinical parameters of the studied older adults

Variables		MMSE		Total
		Normal (n=105)	Abnormal (n=137)	
Gender	Male Female	66 (62.9) 39 (37.1)	42 (30.7) 95 (69.3)	108 (44.6) 134 (55.4)
Agea		68.9 ± 5.97 (71.5 – 64) 67	72 ± 7.4 (77-66) 71	70.66±6.97
Marital status	Married Unmarried	95 (90.5) 10 (9.5)	103 (75.2) 34 (24.8)	198 (81.8) 44 (18.2)
Education Level	Literate Illiterate	93 (88.6) 12 (11.4)	45 (32.8) 92 (67.2)	138(57) 104 (43)
Life situation	With others Alone	97 (92.4) 8 (7.6)	112 (81.8) 25 (18.2)	209 (86.4) 33 (13.6)
TGa		165.9 ± 60.3 (186-128)149	159.9 ± 66 (178-128) 146.5	162.36±63.44
Cholb		197.9 ± 47.4 (230-164.5) 198	196.6 ± 36.8 (223.75-170) 195	197.26±41.65
LDLb		120.1 ± 39.6 (150.5 – 90) 123	119.5 ± 33.2 (140.5-99) 116.5	119.86±36.05
HDLa		45.8 ± 4.9 (50-42.5) 46	45.1 ± 5.4 (49-42) 46	45.47±5.17
Apo Aa		114.8 ± 14.8 (128-106)118	113.2 ± 15.9 (125-106) 116	114.01±15.46
Apo Bb		95.9 ± 26.3 (111-80) 96	92.9 ± 26 (113-79) 92	94.32±26.13
Apo B / Apo Ab		0.83 ± 0.8 (0.99-0.68) 0.81	0.82 ± 0.24 (0.98-0.67) 0.82	0.83±0.23
LP aa		25.1 ± 28.3 (27.35-7) 16.9	26.8 ± 27.9 (31.75-8.72) 17.3	26.04±28.06

Data presented as n(%), mean±std, median [Q1-Q3], aMann whitney Test, b t-test

Table 2. Univariate and multivariate logistic regression

Variables		Univariate		Multivariate	
		OR (95% CI)	P-value	OR (95% CI)	P-value
Gender	Male	reference	--	reference	
	Female	3.828 (2.237-6.550)	<0.001	2.904 (1.497-5.631)	0.002
Agea		1.072 (1.029-1.117)	0.001	1.069 (1.016-1.124)	0.008
Marital status	Married	reference	--	--	--
	Unmarried	3.136 (1.469-6.693)	0.003	--	--
Education Level	Literate	reference	--	reference	--
	Illiterate	15.884 (7.876-31.874)	<0.001	11.417 (5.549-23.492)	<0.001
Life situation	With others	reference		--	--
	Alone	2.706 (1.167-6.277)	0.016	--	--
TGa		0.998 (0.994-1.002)	0.239	--	--
Cholb		0.999 (0.993-1.005)	0.837	--	--
LDLb		1 (0.993-1.007)	0.932	--	--
HDLa		0.976 (0.929-1.026)	0.583	--	--
Apo Aa		0.994 (0.977-1.010)	0.382	--	--
Apo Bb		0.996 (0.986-1.006)	0.402	--	--
Apo B / Apo Ab		0.905 (0.295-2.781)	0.863	--	--
LP aa		1.002 (0.993-1.011)	0.363	--	--

TG: Triglyceride, Chol: Cholesterol, LDL: Low density lipoprotein, HDL: High density lipoprotein, APO A: Apo lipoprotein A, APO B: Apo lipoprotein B, LP a: lipoprotein a, aMann whitney Test, b t-test, Bold p-value are statistically significant

Logistic regression was first performed with individual variables; then, significant variables at the 0.2 level were entered into the multiple logistic regression model, the results of which are shown in Table 2. As can be seen, the variables of age, gender and education level were significant.

Based on the multivariate logistic regression, age, gender, and level of education (OR = 1.069, 95% CI = 1.016-1.124), (OR = 2.904, 95% CI = 1.497-5.631), and (OR = 11.417, 95% CI = 5.549-23.492) played the most crucial role in the cognitive disorders of the older adults.

4. Discussion

Out of the 242 older adults participating in the current study, 43.4% had a normal MMSE, while 56.6% had an abnormal one. In the study conducted by Ahangar et al. (2019), it was reported that 60.4% is the average level. Consistent with the present study, in the study of Hosseini et al. (2016), 34.6% had a normal MMSE, while 65.4% had abnormal MMSE levels [3, 21]. There are studies whose findings part company with those of the current study [22-28]. Some of those studies that reported the prevalence of cognitive impairment include Rait et al.'s (2005) on 15051 Ukrainian older adults (18.3%), Wu et al.'s study (2005) on 2119 Taiwanese older adults (22.22%), Goswami et al.'s (2006) on 1165 Indian seniors (18%), Paul et al.'s (2009) on 1268 Portuguese seniors (9.6%), Rodríguez Sánchez et al.'s (2009) on 327 Spanish seniors (19%), Rashid et al.'s (2011) on 1708 Malaysian older adults (11%), and Kim et al.'s (2012) on 1708 Malaysian older adults (20.5%). Some reasons for this discrepancy in the studies are differences in the study period, age, gender frequency distribution, lifestyle, geographical area, and the sample size. This statistical difference might potentially be explained by a different psychometric procedure for classifying psychological problems in various research. The abnormal MMSE level was significantly higher in women than men. The results of studies by Ahangar et al. (2019), Zunzunegui et al. (2009), Hosseini et al. (2016), Paul et al., and Shin et al. in South Korea were consistent with those of the present study [3, 21, 25, 29, 30]. The higher prevalence of cognitive disorders in women may be related to the longer life expectancy of women than men as with an increase in age, the prevalence of cognitive disorders increases.

The abnormal MMSE level frequency distribution was significantly higher in the older age group than in the younger one. The results of the studies of Ahangar et al. (2019) and Hosseini et al. (2016) were consistent with those of this study [3, 21]. The natural cognitive state of individuals depends on the entire functioning of various brain systems. An increase in age and degenerative changes in the central nervous system

cause dysfunction of the brain and cognitive problems in the individual [29].

The frequency distribution of abnormal MMSE levels in single individuals was significantly higher than in married individuals (P< 0.05). Hosseini et al.'s (2016) findings were consistent with those of this study [21]. According to another research conducted in Iran, living alone is associated with loneliness and depression that could decline cognitive performance [21].

The frequency distribution of abnormal MMSE levels in the older adults was only significantly higher than in the non-older adults. The results of Hosseini et al. (2016) and Ahangar et al. (2019) were consistent with those of the present study [3, 21]. The frequency distribution of abnormal MMSE levels in illiterate older adults was significantly higher than in older adults with high school and university education (P\u003c0.05). The study conducted by Hosseini et al. (2016) was consistent with ours [21].

The mean serum levels of each Apo A, ApoB, Lpa, and Apo B / Apo A ratios were not significantly different in terms of MMSE level in the studied older adults. Bucci et al. (2016) stated that elevated serum Lpa level is associated with the risk of stroke and is a risk factor for this disease [31]. The older adults with elevated serum Lpa may have suffered a stroke and eventually died in the present study. Lpa is an independent risk factor for cardiovascular disease, aortic stenosis, and diabetes [9, 31]. The synthesis of apolipoprotein in hepatocytes genetically influences lipoprotein levels. The mean Lp a level is influenced by the Apo E genotype [9].

The mean serum levels of LDL, HDL, Chol, and TG parameters were not significantly different in normal and abnormal MMSE levels in older adults. In Liu et al. (2018), and also Ahangar et al. (2019) stated that the mean serum levels of cholesterol and LDL in people with Alzheimer's were significantly higher than in the older adults with mild cognitive disorders [3, 32]. The discrepancy in the present research may be in terms of social and race differences of the older people.

Cognitive performance depends on multiple factors such as demographic characteristics, including education level and mood status. Our participants would be different from them. Furthermore, MMSE might not have significant specificity to detect cognitive dysfunction.

Yasuno et al.'s study on 2016 Japanese older adults, Andaloro et al.'s in 2020, Cheng et al.'s in 1889 on Chinese older adults and Yaffe et al.'s on 1037 Iranian older adults showed a significant relationship between high cholesterol and LDL and the incidence of cognitive disorders [13, 33-35]. This is not consistent with the results of the present study. This discrepancy might be due to study time differences, sample size, study population, and lifestyle in different studies.

Wu et al. (2019) found an association among serum levels of LDL and TC with the risk of Alzheimer's disease; this is not consistent with our findings [36]. Among the reasons for this discrepancy are differences in time, the study population in terms of age and gender distribution, lifestyle, method of assessing cognitive disorders, and the type of disease studied. [37]. Hottman et al. (2014) stated that serum HDL levels play a role in cognitive function and neurodegenerative disorders [38]. Serum HDL levels were positively correlated with cognitive function in older adults with Alzheimer's disease [34]. Another study found a significant increase in serum levels of LDL, TG, and Chol in the older adults with Alzheimer's disease compared to those in the healthy group. The mean serum HDL levels in the older adults with Alzheimer's disease significantly decreased [17]. There was also a significant decrease in the control group. This inconsistency between the results might be due to using different cut-off ranges for MMSE in the two studies.

Reducing total cholesterol and low-density lipoprotein levels is a strategy to reduce cognitive impairment in older adults [39]. Studies showed that elevated serum levels of total cholesterol and low-density lipoprotein are associated with an increase in cardiovascular disease, which in turn may increase the risk of cognitive impairment. Reducing brain blood circulation, atherosclerosis, atrial fibrillation, and coagulation disorders can also play a role in Alzheimer's disease and vascular dementia [33].

The limited sample size and lack of research on additional apoproteins such as Apo E are two drawbacks of the present study. Such tests need quantitative data with comparative value, but it is not appropriate for diagnostic purposes, so perhaps it would be better to use two or more tests at the same time to assess the cognitive impairment of the elderly.

Moreover, we did not consider the association among psychological disorders such as depression and cognitive function. It is suggested that future research assess these pathways and interrelationships.

5. Conclusion

The results of present study showed that there is a significant relationship among age, gender, marital

status, level of education, living condition, and MMSE level, so MMSE can be used to improve the cognitive level of the older adults by changing conditions such as marital status, level of education, and life situation. However, no significant relationship was found among Lipid Profile, Apo B/ Apo A ratio, Lp a, and MMSE level.

Ethical Considerations

Compliance with ethical guidelines

All ethical principles are considered in this article. The participants were informed of the purpose of the research and its implementation stages. They were also assured about the confidentiality of their information and were free to leave the study whenever they wished, and if desired, the research results would be available to them. A written consent has been obtained from the subjects. principles of the Helsinki Convention was also observed. This study was approved by the Ethics Committee of the University of Birjand (Code: IR.BUMS.REC.1399.296).

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Author's contributions

Sara Hamdamian. and Asghar Zarban. Concept, design, literature search, Data acquisition and manuscript editing.

Mitra Moodi, Rasoul Raesi and Farshad Sharifi. Data analysis, statistical analysis, and manuscript editing.

Mohammad Dehghani Firoozabadi. Supervision and manuscript review.

All authors read and approved the final manuscript

Conflict of interest

The author(s) declared no potential conflicts of interest.

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