

The Prevalence of Alzheimer's Disease; its Risk and Protective Factors Among the Elderly Population in Iran

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Abstract

Objectives: This study aimed at evaluating the prevalence of the Alzheimer disease and its risk and protective factors in the elderly people referred to health centers in Shiraz, Iran.

Methods: The current descriptive, analytical study was conducted on 2000 elderly by the random sampling method. Mini-mental state exam (MMSE) and geriatric depression scales (GDS) were applied to gather the data. Afterward, the cases with cognitive deficit went through the psychological and neurological examinations. All statistical computations were conducted by SPSS software, version 22.

Results: Of the total number of studied people, 7.85% were identified with cognitive impairment. However, the prevalence of Alzheimer disease was 2.3%. The results indicated that listening to music, having family friends, and the daily consumption of vitamin E were the protective factors, while depression was one of the risk factors in developing the Alzheimer disease.

Conclusions: The findings suggested a unique opportunity for early diagnosis and preventive interventions.

Keywords: Alzheimer Disease, Cognitive Deficit, Aging, Risk Factors, Protective Factors

1. Background

Dementia is one of the prevalent disabilities in the elderly population in aging (1). The world health organization (WHO) has considered dementia as 1 of the 7 neurological diseases with the largest performance gap in the mental health plan (2). The prevalence of mild to severe dementia in the elderly population over 65 is 5%, in people over 85 is 20% to 40%, and those residing in nursing homes is 50% (3). Now, 46.8 million people have dementia and the rate increases doubles every 10 years, as this will reach to 74.7 and 131 million people in 2030 and 2050 respectively (4). Alzheimer is one of the most common reasons of dementia in people aged 60 years and above (5). Alzheimer is a chronic and progressive degenerative disease known with 3 main clinical symptoms. The first group is cognitive decline, the second is behavioral disorders, and the third is disorder in performing daily activities (6). Usually, the lack of memory is the first symptom that appears in Alzheimer, as recent memory has better chance than the long-term memory (7). Often the disorder in multiple domains of cognition appears several years before the clinical diagnosis of Alzheimer. There are many similarities between the cognitive performances at this stage with the normal aging and there is little evidence

ability to identify these clinical changes. Alzheimer is an important cause of morbidity and mortality in the world (8). According to estimates, until 2030, about 30 million people and by 2050, about 45 million people around the world are affected by the Alzheimer disease (9). Different factors raise the risk of Alzheimer or protect the old people from the disease. Some of the treatable risk factors are cognitive, cardiovascular, social, and mental factors as well as lifestyle. Cohort studies report the protective and considerable role of physical activities against Alzheimer. According to a study, the regular physical activity such as walking resulted in better cognitive power (20%) and less cognitive loss in the old females (5, 10). The president of the world Alzheimer's association emphasized the early diagnosis of Alzheimer disease (11). There are 2 important barriers to the necessary and timely policies for Alzheimer disease that may be considered as the lack of prevention and early diagnosis. The lack of studies on the prevalence of Alzheimer is also another barrier that hides the important notes from the eyes of policymakers. Most studies on the prevalence of dementia, Alzheimer, and the risk factors are conducted in the developed countries, while more than 66% of people who are at risk of Alzheimer disease are living in the countries with low and middle incomes, while

only 10% of studies are devoted to these populations (11). Iran should not be excluded from this situation. The failure in the early diagnosis causes the loss of valuable opportunities to improve the quality of life in millions of people with dementia. Moreover, the early cures help the family of patients and their caregivers to use supportive and consulting services. It results in reducing financial, social, mental, and physical costs caused by the disease. The advantages of the early diagnosis are slowing the progression of cognitive decline, maintaining better functional status, reducing the mortality rate, improving the challenging behaviors of the patient, and raising the opportunities for social participations such as recreation, education, and employment (12, 13). Thus, conducting studies to evaluate the prevalence of Alzheimer and presenting them to the policy makers help to specify the dimensions of the disease in the community. In this regard, the current study aimed at evaluating the prevalence of Alzheimer disease, its risk, and protective factors in the old people referred to health centers of Shiraz University of Medical Sciences and the centers supported by the welfare organization of Iran.

2. Methods

The current cross sectional study was conducted during 8 months from February to October 2015 by the convenience sampling method on the elderly people referred to 20 health centers supported by Shiraz University of Medical Sciences and the welfare organization of Iran. The sample size included 2000 people, based on the prevalence of 1%, precision 2%, and error rate (type 1) 5%. The population size in the clinics or centers was determined according to the average number of elderly people referred to the attended clinics or centers. The inclusion criteria were voluntary participation, age of 60 years or above, and the ability to communicate and talk to the interviewer. To collect data, the demographic data questionnaire, mini-mental state examination (MMSE) for the literate and illiterate subjects, and geriatric depression scale (GDS) were applied based on the selected questionnaire (15 questions) to diagnose the depression in the elderly population of Iran. Malakouti et al., standardized the GDS questionnaire and reported the alpha coefficient as 0.9. The cutoff point 8 was obtained for the questionnaire with the sensitivity of 90% and specificity of 84% (14). According to the pretest applied to 50 elderly patients, the cutoff point of the test in the current study was 8. The MMSE included 10 questions with total score 30 and regarded as one of the most common tools to measure the general cognitive function. It was designed by Folstein et al. (15) and now it is considered as the most common screening tool in the world for investigating the cog-

nitive status of the old people (16). The reliability and validity of the test were evaluated by Folstein et al. The validity of the test was $\alpha = 0.78\%$ and in the pretest, its sensitivity and specificity were 100% and 84%, respectively (16). The pretest applied to 50 elderly patients also showed a validity of $\alpha = 0.921$. The mini-mental cognitive state examination for the illiterate people was conducted. The Persian form of the test was developed by Gholamzadeh Basit to screen the cognitive status of the low-literate/illiterate elderly. The reliability of the test was assessed by two methods: the evaluation of the internal validity and the correlation between the two forms. The Cronbach's alpha values were 0.92 and 0.96, respectively (17). The validity of the test according to the pretest on 50 elderly patients was $\alpha = 0.896$. In the current study, the values of cutoff point, sensitivity, and specificity for the illiterate cognitive weakness test were 22.5, 94% and 98%, respectively; while, for the literate participants, they were 22.5, 94% and 73%, respectively. In addition, the cutoff point recommended by the agency for health care policy and research (AHCPR) was also applied (Table 1). The suspicious elderly referred to the psychologist and, then, neurologist with regard to their cognitive status score under the cutoff point recommended by AHCPR. The neuropsychometric examination was used for the people referred to the psychologist. Finally, they referred to the neurologist for their definitive diagnosis of Alzheimer by the blood tests and brain magnetic resonance imaging (MRI) examination.

3. Results

Most of the participants were male (54%), married (80.1%), holding the elementary education (39.5%), and retired (43.9%). About 1.20% of them were divorced and 14.6% had university degrees. The mean and the standard deviation of the age were 67.4 ± 6.44 years. The most common underlying diseases among the participants were high blood pressure (45.2%), hyperlipidemia (33.4%), and diabetes (28.9%). The most common drugs consumed by the participants were antihypertensive (45.2%), aspirin (36.2%) and anti-lipid (28.3%).

According to Table 2, the prevalence of cognitive weakness in the illiterate and literate groups as well as total population was 3.95%, 3.9%, and 7.85%, respectively.

However, according to the cutoff point of the AHCPR guidelines, the distribution and prevalence of the cognitive impairment in various age and education groups was 30% (n = 602). The prevalence of cognitive impairment in the elderly with less or no education (illiterate), primary/elementary level, high school, and university degree were 5.5% (n = 110), 14.15% (n = 283), 6.05% (n = 121), and 4.4% (n = 88), respectively (Table 3).

Table 1. The Cutoff Point of Mini-Mental Examination, Based on the Age and Level of Education^a

Age Group, y	Illiterate	Primary School	Under Diploma	University
60 - 64	22	27	29	29
65 - 69	22	28	28	29
70 - 74	21	26	28	
75 - 79	21	26	27	
80 - 84	19	25	26	28

^aValues are expressed as number.

Table 2. Cognitive Weakness Among the Studied Elderly, Based on the Educational Level

Status	Number	Percentage	Total Percentage
Literate, (Cutoff point: 22.5 and less)			
Unhealthy	78	5.4	3.9
Healthy	1365	94.6	68.25
Total	1443	100	72.15
Illiterate, (Cutoff point: 19.5 and less)			
Unhealthy	79	14.2	3.95
Healthy	478	85.8	23.9
Total	557	100	27.85
Total	2000		

Despite the free visits and tests for the diagnosis and cure of the elderly people with cognitive weakness ($n = 602$), only 126 participants agreed to visit the specialists. For the subjects referred to the psychologist ($n = 126$), the psychometric examination was used and it was reported that most of the subjects (70.3%) had major depression, only 11 subjects (8.8%) were diagnosed with dementia, and 33 persons were diagnosed with mild cognitive impairment. Out of the 59 elderly patients entitled to visit the neurologist, only 26 subjects referred to the clinic for the examination. Blood tests including complete blood counts (CBC), liver and kidney function tests (KFT), and serum levels of homocysteine, B12 level, as well as brain MRI were performed on them. Based on the neurologist's diagnosis, the results indicated 10 cases of Alzheimer, 9 with B12 deficiency, and 7 with primary psychiatric mood disorder. However, 31 subjects (1.2%) refused to visit the specialist for further evaluation.

Based on the results, MMSE and GDS scores were significantly correlated, $R = 0.344$, $P < 0.01$. MMSE score and weekly hours of visiting friends were also significantly correlated, $R = 0.107$, $P < 0.01$. However, other variables such as level of education and weekly hours of visiting the family showed no significant relationship with MMSE scores. The Pearson correlation coefficient analysis also indicated a significant inverse relationship between the cognitive deficits and depression. Multiple regression analysis was used to evaluate if these 3 variables significantly predicted cognitive impairment of MMSE score.

The results of the regression indicated that the 3 predictors explained 19.3% of the variance ($R^2 = 0.193$, $F_{(3,1938)} = 15.33$, $P < 0.01$) in MMSE scores. It was found that MMSE score significantly predicted ($\beta_0 = 37.622$) by GDS score ($\beta_1 = -0.258$, $P < 0.01$), age ($\beta_2 = -0.147$, $P < 0.01$), and weekly hours of visiting friends ($\beta_3 = 0.042$, $P < 0.01$). The logistic regression indicated that depression was one of the risk factors for Alzheimer in the elderly. The other diseases such as heart diseases, diabetes, thyroid dysfunction, arthritis, migraine, hyperlipidemia, and cancer had no effects on the development of Alzheimer in the subjects of the current study.

The results of the logistic regression indicated that listening to music explained 6.428 of the variance in MMSE score (Wald = 6.428, $P < 0.05$, $\beta = 0.317$). In addition, about the effect of medications, the result of the logistic regression revealed that consumption of vitamin E explained 6.89 of variance in MMSE score ($P < 0.05$, Wald = 6.897, $\beta = 0.847$) (Table 4).

The logistic regression indicated that daily listening to music was assumed as the protective factor against the prevalence of cognitive impairment (Table 5).

Based on the regression analysis daily listening to music and consumption of vitamin E were the protective factors against cognitive impairments (Table 5). However, there was no significant relationship between the score of cognitive impairments and other factors.

Table 3. Frequency and Percentage of Mini-Mental Score, Based on the Age and Educational Level of the Study Participants

Age Group, y	Education									
	Illiterate			Primary school		Diploma		University		
	Cutoff point		Distribution	Cutoff point	Distribution	Cutoff point	Distribution	Cutoff point	Distribution	Cutoff point
60 - 64	22	No.	26	27	99	29	71	32	32	32
		%	1.3		4.95		3.55		1.6	
65 - 69	22	No.	25	28	94	28	70	24	24	1.2
		%	1.25		4.7		0		1.2	
70 - 74	21	No.	24	26	41	28	16	24	24	1.2
		%	1.2		2.05		0		1.2	
75 - 79	21	No.	17	26	32	27	10	4	4	0.2
		%	0.7		1.6		0		0.2	
80 - 84	19	No.	15	25	15	28	0	4	4	0.2
		%	0.75		0.75		0		0.2	
> 85	20	No.	6	24	2	28	1	0	0	0
		%	0.3		0.1		0.05		0	
Total		No.	110		283		88		88	4.4
		%	5.5		14.15		4.4		4.4	

Table 4. The Regression of Logistic Model to Determine the Effect of Lifestyle Factors and Drug Consumption on the Prevalence of Alzheimer in the Elderly

Variable	Cutoff	S.E	Wald	Exp. (B)	C.I. for Exp. (B)			
					Lower	Upper		
Listening to music	-0.317	0.125	1	0.011	0.728	0.570	0.931	
Exercise	-0.043	0.126	0.11	0.730	0.957	0.748	1.266	
Smoking	0/309	0.218	2.01	0.157	1.362	0.888	2.090	
Access to water pipe	0.082	0	0	0.769	1.086	0.626	1.883	
Alcohol consumption	0.576	0	1.01	0.288	1.778	0.614	5.146	
Drinking tea/coffee	-0.173	0.204	0.720	1	0.396	0.841	0.563	1.255
Constant	-1.291		38.633	1	0.000	0.275		
Anti-hypertensive	-0.067	0	0.15	1	0.613	0.935	0.720	1.214
ASA	-0.062	0.132	0.218	1	0.641	1.363	0.821	1.378
Anti-lipid	-0.17	0.144	0.034	1	0.853	0.948	0.734	1.291
Hypoglycemic agent	-0.146	0.146	0.002	1	0.993	0.961	0.745	1.322
Vitamin D	-0.271		1.258	1	0.262	0.763	0.457	1.224
Analgesic	0.483	0.452	1.142	1	0.285	1.621	0.891	2.084
Antacid	-0.054	0.254	0.045	1	0.833	0.948	0.576	1.560
Vitamin E	0.847	0.323	6.897	1	0.009	2.333	1.240	4.389
Cortisone	-0.385	0.254	2.542	1	0.111	1.849	0.869	3.936
Narcotic	-0.217	0.205	1	0.154	1.363	0.668	3.931	
Proton pump inhibitor	0.004	0.794	0.000	1	0.996	1.004	0.212	4.760
Constant	-1.656	0.096	295.270	1	0.000	0.191		

4. Discussion

The current study aimed at evaluating the prevalence of Alzheimer among the old people in Shiraz by MMSE

screening tools. This study was the most comprehensive study conducted in Iran to estimate the exact values of Alzheimer prevalence.

The results indicated that according to AHCPR guide-

Table 5. Protective and Risk Factors of Cognitive Impairment Among the Study Population, Based on Lifestyle

Variable	Sig	Odd's Ratio	OR	Lower	Upper
Listening to music	0.011	0.728	0.272	0.930	1.000
Exercise	0.730	0.957	0.730	1.000	1.000
Smoking	0.157	1.362	0.888	1.000	1.000
Access to water pipe	0.769	1.086	0.26	1.883	1.000
Alcohol consumption	0.288	1.778	0.614	5.146	1.000
Drinking tea/ coffee	0.396	0.841	0.563	1.255	1.000
Anti-hypertensive	0.613	0.935	1.214	1.000	1.000
ASA	0.641	1.000	1.378	1.000	1.000
Anti-lipid	0.853	1.000	1.291	1.000	1.000
Hypoglycemic agent	0.993	0.961	0.745	1.322	1.000
Vitamin D	0.262	0.763	0.457	1.224	1.000
Analgesic	0.285	1.621	0.891	2.084	1.000
Antacid	0.833	0.948	0.576	1.560	1.000
Vitamin E	0.009	2.333	1.240	4.389	1.000
Cortisone	0.111	1.000	0.869	3.936	1.000
Narcotics	0.154	1.000	0.668	3.931	1.000
Estrogen	0.900	1.004	0.212	4.760	1.000

lines, the cognitive weakness prevalence in different age and education groups was 30.1%, although according to neurological examination and brain MRI, the Alzheimer was diagnosed in 2.3% of the studied population. The abovementioned results conformed to those of previous researches. In a study conducted on the non-Caucasian elderly by White, the prevalence was reported almost double by the mini-mental scale (18). In Egypt, Ragab et al., also reported that the dementia prevalence was doubled (19). Chandra et al., reported the dementia prevalence in the population over 65 years old as 15.4% (19). In Hong Kong, Lam et al., and in Rotterdam Ott et al., reported the dementia and Alzheimer prevalence in the population over 70 years old as almost triple (19-22). In the current study, the most important concern was that the elderly who should have definitely referred to the research centers refused attending. Among the variety of studies on the prevalence of Alzheimer and dementia, Rotterdam research is considered as a study with the highest participation of old people (about 80%). The consequences of lack of participation in these examinations, which are less than 20% values for the prevalence of Alzheimer (22).

The present study indicated that daily listening to music is one of the protective factors against the Alzheimer in the old people. In the study by Lipe et al. (23), a significant

relationship was reported between MMSE score and music. It should be mentioned that its findings conformed to the current study results. Cognition improvement should be expected with the utilization of music treatments due to its anxiolytic effects. Based on the studies, listening to music reduces anxiety and thereby enhances the elderly's cognitive function (24). Interventions, which decrease anxiety, lead to significant and rapid decline in the elderly's cognitive function (25-27).

In addition, the current study results indicated that the daily consumption of vitamin E was one of the protective factors against Alzheimer disease. Morris et al., reported results similar to those of the current study (28). A recent study indicated that the combined consumption of vitamin E 400 IU daily and vitamin C 500 mg daily for at least 3 years was correlated with a lower incidence of Alzheimer disease (28, 29). Scientifically, antioxidants such as vitamins C and E may help to prevent the oxidation of cysteine that leads to change in the structure and function of the modified tau protein normally located within neurofibrillary tangles of the brain in patients with Alzheimer (30); although the other drugs such as the antihypertensive, aspirin, anti-lipid, blood sugar, vitamin D, analgesics, anti-acid, corticosteroid, narcotics, and estrogen had no effect on Alzheimer in the studied population.

Unlike the findings of the current study on the lack of relationship between hormone therapy and the cognitive test score, Iranmanesh et al., reported a significant difference in the average scores of cognitive test between people who consumed estrogen and the ones who used progesterone. But, there are still conflicts on the hormone therapy among the researchers due to its disadvantages (31). According to Wolozin, the consumption of 3-hydroxy 3-methyl-coenzyme A drug group, such as atorvastatin and simvastatin, had protective effects on the emergence of Alzheimer. According to the results of previous studies, it seems that the consumption of these drugs is reasonable (32). Unlike the current study, Stumer et al., reported the protective effect of aspirin on the studied population as they measured the possibility of Alzheimer development in the aspirin consumers as 97% (33). Although Yeshokumar et al., reported a relationship between the low levels of 25-hydroxy vitamin D in blood and the increased risk of Alzheimer; no significant relationship was found in the current study (34).

About the risk factors of Alzheimer disease, the current study results also indicated that the depression was one of the risk factors for Alzheimer among the studied elderly. The findings of Winter et al., also confirmed the current study results. They also reported the increased risk of Alzheimer in the presence of depression (35). Results of correlation coefficient indicated a significant and inverse relationship between the cognitive weaknesses and age. The relationship between cognitive impairment and age was significant in the studies by Paul et al. (36), Min et al. (37), and Sohrabi et al. (38).

Also, the results of correlation coefficient indicated a significant relationship between the cognitive impairments with the weekly visiting hours with friends. Consistent with the current study, Beland et al., reported that having friends was significantly correlated with cognitive function changes in the elderly (39). Previous studies demonstrated a positive correlation between the perceived social support and general cognitive function in older people (40, 41). These findings were compatible with those of previous studies, which indicated that social interaction and having friends are related to cognition, even at later age (42, 43).

However, there was no significant relationship between the visiting hours with family, family size, and cognitive impairment. Litwin et al., proposed that friends have positive and protective effects on older adults as the relationship with the family is less. This differs from family relationships in which contact may not be based on choice. However, in another study family support was the major predictor of cognitive function (44); the difference is probably owed to the heterogeneity of family support among the

Iranian older people.

There was no significant relationship between the score of cognitive weakness test and the studied factors such as body mass index (BMI), mother's age, mother's age, family size, the age difference between the participant and his/her first child, and the number of siblings. Unlike the findings of the current study, in other studies, there was a correlation between cognitive decline, low or low body weight (45). Despite the findings of the current study, Rocca et al., (46) reported that the age above 40 years for the mothers was regarded as a risk factor for predisposing to Alzheimer in children during old ages. Many participants in the current study were born from the very young and young mothers. The mentioned findings could not be generalized to the study. In addition, Ott et al., (22) reported that the high age of the father at the time of birth and the late age of marriage are the risk factors for developing Alzheimer, although they indicated a weak relationship between the age of mother and Alzheimer disease. Unlike the findings of the current study, Moceri et al., (47) evaluated the conditions of the first 18 years of life in patients with Alzheimer. According to this study, the risk of Alzheimer in the child is added to the family. Perhaps, the reason of difference between findings is related to the studied population, the kind of tools and cultural differ-

ences. In the comparison between the averages indicated that the old people with high blood pressure, stroke, head injury, heart disease, depression, arthritis, and peptic ulcer had different cognitive scores, compared with healthy people. Perhaps, it was due to the drugs consumed by them. In the study by Lindsay et al., (48) development of arthritis and the consumption of nonsteroidal anti-inflammatory drugs (NSAIDs) were reported as the protective factors against Alzheimer. Also, the risk of Alzheimer in the old people who consumed NSAIDs reduced to 35% (45). The old people who consumed the antihypertensive and anti-acid drugs, as well as analgesics had different scores in the cognitive test than the old people who consumed no drugs. That relationship was not significant in the studies by Lindsay (48). It might be related to the difference (in percentage) of people who consumed the blood pressure lowering drugs in both research communities. Olichney et al., (49) evaluated the relationship between brain stroke and Alzheimer. They reported the risk value of 3.5 based on the regression model. Their findings were the same as the current study results. In another study by Forette et al. (50), consuming drug for high blood pressure and reducing the diastolic blood pressure on the average score of MMSE was significant. The statistics indicated that following the treatment of 1000 people with high blood pressure during 5 years, the emergence of 19 new cases was prevented. The

findings were consistent with those of the current study. Luukenin et al., (51) reported no significant relationship between the mild concussion and the MMSE score, but a positive relationship was found between severe concussion and the loss of MMSE score. McGeer et al., (52) in a study similar to the current survey achieved the same results on the protective effects of arthritis and the consumption of anti-inflammatory drugs to control the inflammatory symptoms against the Alzheimer disease. Also, according to the results, there was a significant difference in the average score of cognitive weakness test between the elderly males and females, and the cognitive weakness was more in the females.

Ott et al., reported a significant difference in the score of cognitive weakness test between the genders. This result was similar with that of the current study findings (22). Also, the cognitive weakness varied among different education groups and the findings indicated that the cognitive weakness was more in the illiterate elderly and less in the elderly with the university degree. Stern et al., (53) and Cobb et al., (54) achieved the same findings on the negative effect of lower levels of education on the risk of Alzheimer. Lindsay, Plassman, and Tyas also found a significant relationship between the education and the score of cognitive test. The findings were the same as the current study results (48, 55, 56). The results of a research conducted by Masoomi et al., were the same as those of the current study. It showed the positive effect of education on the dimensions of cognitive status such as data registration, attention and calculation, remembering, and the language skills (57). Also, there was a significant relationship between the cognitive weakness and the marital status. The cognitive weakness was higher in the elderly women than other groups. Masoomi et al., (57) reported a significant difference in the score of cognitive weakness among groups with various marital status. The findings of that study were similar with those of the current study.

Although the current study had many strengths, there were some limitations that made it difficult to generalize it to the other populations. Most of the tests and evaluations on the protective factors and Alzheimer risk were conducted according to the score of semi-mental tests for the cognitive weakness, while the semi-mental tools are not enough for the definitive diagnosis of Alzheimer. The cognitive as well as psychometric and neurologic tests are also required for the definitive precise diagnosis. Unfortunately, the limitations of the current study, reflected by many experts in the cognitive weakness, remained at the specialists. Thus, it is recommended that the plans and policies on prevention, screening, and the treatments of Alzheimer disease are made both in national and regional levels.

4.1. Conclusion

It was concluded that the prevalence of cognitive impairment and Alzheimer disease in the elderly study population was lower than those of other countries. Education was the most significant risk factor, and listening to music, the weekly visit with friends, the consumption of vitamin E were the most important protective factors against Alzheimer disease. The above-mentioned results showed the need to plan and implement programs for the high-risk groups and also conduct more vast researches in the regional and national levels.

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Footnote

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