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An Investigation of the Risk Factors and Prevalence of Alzheimer's Disease in the Eastern Region of Turkey

A Population Based Door-to-Door Survey

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ABSTRACT

The relationships between the prevalence of AD, socio-demographic characteristics, and other chronic diseases were researched within the population aged 65 and over living in Erzurum city center. The study was realized between June of 2010 and July of 2011. It involved 455 people over age 65 living in Erzurum city center. The Mini-Mental State Examination and Daily Living Scale were applied to participants. A total of 455 people participated in the study. AD was detected in 29 people. Twenty-one participants were female, and eight were male. The prevalence of AD was calculated to be 6.4%. According to the results of a logistic regression analysis, the AD prevalence detection rate in the a 75-84 age group was ten times greater than in the 65-74 age group, and the rate in the 85 and over group was 36 times greater than in the 65-74 age group. AD is more common in women than in men. The rate increases 4.1-fold among those with AD diabetes mellitus disease, 3.9-fold among those with Parkinson's disease, 2.6-fold among those with heart disease, and 4.2-fold among those with dementia in their families. AD prevalence for those age of 65 and over was shown to be 6.4% in our study. The risk of AD increases 17-fold with increasing age. The risk of developing AD also increases in cases of chronic diseases.

Key words: *Alzheimer's disease, prevalance, epidemiology, risk factors*

Türkiyenin Doğu Bölgesinde Alzheimer Hastalığının Prevalansı ve Risk Faktörlerinin Araştırılması

Toplum Dayalı Kapı Kapı Bir Çalışma

ÖZET

Demans, bellek bozukluğuna lisan, yönelim, praksi, soyut düşünme, problem çözme gibi bilişsel işlevlerden en az birinin eşlik etmesiyle iş ve sosyal yaşamda fonksiyon kaybının ortaya çıkmasıdır. Tüm demans olgularının %50-70 'ini Alzheimer hastalığı (AH) oluşturmaktadır. Erzurum il merkezinde yaşayan 65 yaş ve üzeri popülasyonda AH prevalansı, sosyodemografik özellikleri ve kronik hastalıklar ile olan ilişkisi araştırıldı. Çalışmaya haziran 2010 - temmuz 2011 tarihleri arasında Erzurum il merkezinde yaşayan 65 yaş ve üzerindeki 455 kişi alındı. Katılımcılara Mini Mental Durum Muayenesi ve Günlük Yaşam Ölçeği uygulandı. Çalışmamıza toplam 455 kişi katıldı. AH 29 kişide tespit edildi. 21'i (%9.3) kadın, 8'i (%3.5) erkekti. AH prevalansı %6.4 olarak hesaplandı. AH tanısı alan grubun yaş ortalaması 80,8±9.1 iken, sağlam grubun yaş ortalaması ise 71.1± 6.1 idi. İki grup arasında yaş dağılımı açısından istatistiksel olarak anlamlı bir fark bulundu (p< 0.001). Logistik regresyon analizi sonuçlarına göre; AH prevelansı 75-84 yaş grubunda, 65-74 yaş gruba göre yakalanma oranı 10 kat, 85 yaş ve üzeri yaş grubunun ise 65-74 yaş grubuna göre AH yakalanma oranı 36 kat daha fazla bulundu. AH kadınlarda erkeklerden daha fazla görülmektedir. AH diabetes mellitus hastalığında 4.1, parkinson hastalığında 3.9, kalp hastalığında 3.6, ailesinde demans olanlarda olmayanlara göre 4.2 kat istatistiksel olarak artmaktadır. Çalışmamızda 65 yaş ve üzeri AH prevalansı %6.4 idi. Yaş ilerledikçe AH'ı 17 kat arttığı görüldü. Aynı zamanda kronik hastalıklarda AH gelişme riski artmaktadır.

Anahtar kelimeler: *Alzheimer Hastalığı, prevalans, epidemiyoloji, risk faktörleri*

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INTRODUCTION

It is estimated that there are 146 million people aged 65 and over in developed countries around the world, and it is predicted that this age group will be around 232 million in 2010 and 1.4 billion in 2030 (1). According to the estimates of the World Health Organization, Turkey's total population will continue to grow for the first half of this century, and it will exceed 103 million by 2050. Although 4.5% of Turkey's population was over the age of 65 in 1997, this percentage will increase to 20.2% by 2050 (2). Because of this growth, an increase will also occur in the number of people with dementia and mild cognitive impairment (3). Fifty to seventy percent of all dementia cases are cases of Alzheimer's disease (AD). The frequency of AD doubles every five years. There is no adequate epidemiological research regarding this issue in Turkey. However, it is now known that there is a strong relationship between AD and vascular risk factors (4-6).

In this study, we aim to determine the AD prevalence in the population aged 65 and over living in the city center of Erzurum, its socio-demographic characteristics, and its relationship to other chronic diseases.

MATERIALS AND METHODS

This study examined people aged 65 and over living in the city center of Erzurum. We assumed that 5% was the lowest possible AD prevalence. For this reason, it was accepted as the base value when determining the target population. The minimum sample size formula was used to determine the number of people sampled. The prevalence of Alzheimer's disease used in determining the sample size was (p) %5 d = 2. Within a 95% confidence interval, the sample size was calculated to be 455 by using the n=Nt2p.q/d2(N-1)+t2pq formula.

One hundred and twenty-one family doctors were working in the city center of Erzurum, and a population of approximately 3,000-3,200 people were dependent on each family doctor. Using a simple randomized method, 30 physicians were selected, and each one was considered as a cluster. After 14-15 people were included in each cluster, face-to-face interviews were performed by going door-to-door. The purpose of the study was explained, and a questionnaire was given to those who voluntarily agreed to participate to the study.

A questionnaire form researching the socio-demographic characteristics of the participants and their risk factors for AD was filled in. Age, gender, marital status, education and socio-economic status, occupation and employment status, and systemic diseases (hypertension, diabetes mellitus, heart disease, cerebrovascular disease, Parkinson's disease, thyroid disease, psychiatric illnesses, a brief history of head trauma, dementia history in family, smoking, and alcohol consumption) were recorded on this form.

Cognitive impairment was examined by using a structured form to detect the participant's cognitive function disorders, and the Standardized Mini Mental State Examination (MMSE), the most commonly used cognitive screening test for both the educated and uneducated, was applied. In our study, 19/20 MMSE points for the uneducated and 23/24 MMSE points for the educated were accepted as the threshold values for dementia.

Those had cognitive impairments according to their MMSE scores were re-evaluated by the neurology assistant who administered the MMSE test. Physical and neurological examinations were performed. The DSM-IV diagnostic criteria were used in the diagnosis of Alzheimer's disease.

According to the DSM-IV diagnostic criteria for dementia, cognitive loss must be accompanied by social and occupational function loss. It is thought that cognitive tests are not sufficient to diagnose dementia, especially in societies with lower education levels. Cognitive test scores may decrease in patients without functional loss. Therefore, in all cases, functional impairment was also evaluated according to the Global Deterioration Scale (GDS). The GDS is a tool with a seven-stage classification system for grading cognitive and functional capacity along a spectrum that ranges from normal ageing to violent dementia. No neuropsychiatric test or scale was used except the Global Deterioration Scale (GDS) (7) grading because it provides a complete clinical assessment. The GSD scale is as follows: 1-2 indicates normal function, and 3 indicates mild cognitive impairment. Three points and more is considered the limit of dementia (8).

Statistical analysis

The data analysis was performed by using SPSS 20 software. Data were given in terms of number, percentage, mean, and standard deviation. This analysis was performed in two stages. During the first stage, one-variable (univariate) analysis was performed. In these analyses, the Chi-square (x^2) test, Chi-square trend test, Fisher's

Table 1. *Gender distribution of the participants according to the age group*

Age groups (years)	*Woman n (%)*	*Man n (%)*	*Total n (%)*
65-74	*151 (33.1)*	*17 (37.9)*	*323 (71)*
75-84	*60 (13.1)*	*49 (10.9)*	*109 (24)*
85 ve +	*14 (3.1)*	*9 (1.9)*	*23 (5.1)*
Total	*225 (49.5)*	*230 (50.5)*	*455 (100)*

exact test and Student t-test were used. During the second stage, multivariate analysis was performed to demonstrate the risk factors affecting AD. A logistic regression analysis was used for this multivariate analysis. Gender, age group, marital status, educational level, family history, heart disease, diabetes, cerebrovascular disease, and Parkinson's disease were used as independent variables within the model. The odds ratios and p values of the variables were calculated within a 95% confidence interval. The statistical significance level was taken to be $p<0.05$.

RESULTS

In the study, there were 455 people aged 65 and over living in the city center of Erzurum. Two hundred and twenty-five (49.5%) of the participants were female, and 230 (50.5%) of the participants were male. There were 323 people aged 65-74 (71.0%), 109 people aged 75-84 (24.0%), and 23 people (5.1%) aged 85 or over (Table 1). The average age was 71.7 ± 6.8. Two hundred and fifty-four (55.8%) of the participants had hypertension, 120 (26.4%) had heart disease, 86 (18.9%) had diabetes, and 15 (3.3%) had psychiatric disorders. Also, 265 (58.2%) of the 455 people did not smoke, and 141 (31.0%) smoked previously. Four hundred and thirty-one people (94.7) did not use alcohol, and 24 (5.3%) had left alcohol. The number of people whose first-degree relative had dementia was 34 (7.5%). Two hundred and five (45.1%) of the participants had amnesia, 90 (19.8%) had a loss of abstract thinking, and 80 (17.6) had incontinence. AD was detected in 29 people. The prevalence of AD was calculated to be 6.4%. The number of those without a diagnosis of AD was 426 (93.6%). The average age of those diagnosed with AD was 80,8±9.1, while the average age of those who were not was 71± 6.1. A statistically significant difference was found in terms of the age distributions of the two groups ($p<0.001$).

There were three (2.0%) women and two (1.2%) men in the 65-74 age group, 14 (23.3%) women and four (8.2%) men in the 75-84 age group, and four (38.6%) women and two (22.2%) men in the 85 and over age group with a diagnosis of AD. The incidence of AD later in life increases for both sexes, but it increases more greatly for women (Table 2). The incidence of AD increases in both sexes as age increases over 85 years.

According to the GDS for both sexes, there were no advanced-stage AD patients in the 65-74 age group, but the number of patients with advanced-stage AD increased in the 75-84 and 85 and over age groups.

A statistically significant relationship between level of education and AD was found ($p<0.001$). When level of education increased, AD decreased. A statistically significant difference between the retired housewifes and AD was found ($p<0.001$) (Table 3).

According to the results of the univariate analysis, the frequency of AD incidence in patients with HT was increased compared to those without HT disease. However, this was not statistically significant ($p>0.05$). In cases of diabetes, heart disease, cerebrovascular disease, and Parkinson's disease, AD frequency was increased ($p<0.05$). The frequency of AD incidence in patients with a history of head trauma, mental disorders, or thyroid diseases did not increase. In our study, no statistically significant correlation was found between smoking, alcohol use, and AD.

Table 2. Age groups for AD and its distribution according to the gender

	Alzheimer's disease (AD)			
	There is		*Non*	
Age groups (years)	*Woman n (%)*	*Man n (%)*	*Woman n (%)*	*Man n (%)*
65-74	*3 (2)*	*2 (1.2)*	*148 (98)*	*170 (98.8)*
75-84	*14 (23.3)*	*4 (8.2)*	*46 (76.7)*	*45 (91.8)*
85 and +	*4 (28.6)*	*2 (22.2)*	*10 (71.4)*	*7 (77.8)*

Table 3. Comparison of socio-demographic characteristics of the participants and AD

Socio-demographic characteristics		There is AD n (%)	Non AD n (%)	Total n (%)	p value
Gender	Woman	21 (9.3)	204 (90.7)	225 (100)	0.01
	Man	8 (3.5)	222 (96.5)	230 (100)	
Age groups					
	65-74	5 (1.5)	318 (98.5)	323 (100)	<0.001
	75-84	18 (16.5)	91 (83.5)	109 (100)	
	85 ve +	6 (26.1)	17 (73.9)	23 (100)	
Marital status					
	Married	10 (3.5)	279 (96.5)	289 (100)	0.03
	Single	0 (0)	2 (100)	2 (100)	
	Widoved, divorced, separated	19 (11.6)	145 (88.4)	164 (100)	
Education					
	Illiterate	23 (13.6)	146 (86.4)	169 (100)	<0.001
	Literate	2 (2.2)	88 (97.8)	90 (100)	
	Primary school	4 (3.4)	115 (96.6)	119 (100)	
	Secondary school, high school, college	0 (0)	77 (100)	77 (100)	
Working condition	Housewife	20 (9.6)	189 (90.4)	209 (100)	0.02
	Retired	9 (4.0)	214 (96)	223 (100)	
	Working	0 (0)	23 (100)	23 (100)	
Profession					
	Housewife	21 (9.7)	196 (90.3)	217 (100)	0.005
	Worker	6 (7.0)	150 (98.7)	152 (100)	
	Other (official, etc.)	2 (1.3)	80 (93.0)	86 (100)	
Working with manual labor					
	Housewife	20 (9.5)	190 (90.5)	210 (100)	0.02
	There is	5 (5.4)	87 (94.6)	92 (100)	
	Non	4 (2.6)	149 (97.4)	153 (100)	
Economic situation	Bad	1 (4.5)	21 (95.5)	22 (100)	0.13
	Medium	26 (7.7)	312 (92.3)	338 (100)	
	Good	2 (2.1)	93 (97.9)	95 (100)	

AD: Alzheimer's disease p: pearson's coefficient for fulfill the cells requirements statistical (≤%20) for chi-square test (x^2) was analyzed by combining some of the options.

According to the results of the logistic regression analysis, the AD detection rate in the 75-84 age group was found 10 times higher than that in the 65-74 age group, and in the 85 and over age group, this rate was found to be 36 times higher than in the 65-74 age group (p<0.001). At the same time, the AD detection rate was increased 4.1 times for those with diabetes, 3.9 times for those with Parkinson's disease, 3.6 times for those with heart disease, and 4.2 times for those having dementia in their family (Table 4).

DISCUSSION

Alzheimer's disease is the most common type of dementia. It constitutes 50-60% of all dementia cases. Its prevalence increases in direct proportion with age (9). In a study of Turkish Alzheimer prevalence conducted in Istanbul, AD prevalence was found out to be 11% among those over 70 years of age (10). Rochwood et al. (11) reported that dementia prevalence was 2.2-8.4 % for those 65 years of age and over, 10.5-16% for those 75 years of age and over, and 15.2-38.9% for those 85 years of age and over according to a meta-analysis of 17 studies in many regions of the world. In this study, prevalence of Alzheimer's disease was found in accordance with that seen in the literature: 6.4%.

AD is a disease that leads to increased dementia. It is reported in all community-based studies conducted using standards-based criteria that dementia increases exponentially with age (12,13). In our study, there was a statistically significant difference between age groups regarding AD. The prevalence of AD increased with advancing age. Although it is reported in most studies that AD frequency is higher in women, there are some studies that oppose this view (12,13). It has been put forward that AD is more common in women because women live

Table 4. Effects on AD of age groups and some chronic diseases as a risk factor: the results of logistic regression analysis

Risk factors	*Exp(B) (Odds Rate)*	*95% CI for Exp(B)*	*p value*
Diabetes mellitus	*4.136*	*1.495-11.443*	*0.006*
Parkinson disease	*3.988*	*1.201-13.248*	*0.024*
Family history	*4.263*	*1.157-15.708*	*0.029*
1.Age Gorup (65-74)			*<0.001*
2.Age Group (75-84)	*10.508*	*3.242-34.060*	*<0.001*
3.Age Gorup (85 and +)	*36.124*	*7.295-178.893*	*<0.001*
Sex	*0.793*	*0.267-2.356*	*0.676*
Education	*2.772*	*0.743-10.337*	*0.129*
Cerebrovascular Disease	*1.650*	*0.449-6.059*	*0.451*
Heart Disease	*3.675*	*1.329-10.168*	*0.012*
Marital Status	*0.838*	*0.303-2.317*	*0.733*

Changeable(s): diabetes, parkinson dis., family history, age group, sex, education, cerebrovascular dis., heart disease, marital status. CI: Confidence Interval

longer. There are also publications that associate AD frequency with the lower average education levels of women. Many studies have been published showing that the annual incidence of dementia in women is greater than that seen in men (13-15). In our study, although a statistically significant relationship was found between gender and AD in our univariate analysis, no significant relationship not found according to the multivariate logistic regression analysis.

Low levels of education increase the possibility of developing AD. The mechanism by which a high level of education has a protective effect regarding AD is not known (16). A 75-year-old person who is uneducated is two times more likely to develop AD than someone who is the same age and has at least 8 years of education. In most studies, a low level of education was reported to be a risk factor for AD (17-19). In our study, AD rate was found to be increased in the illiterate group. A statistically significant relationship was found between a low level of education and the detection rate of AD.

Those who have jobs that do not require cognitive activity are at a high risk of developing AD, regardless of the level of education (15). When profession group and work performance are taken into consideration, it has been found that the rate of AD is higher among those who are retired workers or housewives than among other profession groups (retired officers, etc.) and those who are still working; this relationship has been found to be statistically significant.

Married and unmarried people were included in a study, and their cognitive impairment levels were researched. Cognitive impairment was greater for those who were unmarried than those who were married (20). The incidence of AD was greater for those who were widowed than that of the married group and the single group. However, no statistically significant association was found between marital status and AD. This situation suggests that being widowed is a limiting factor in terms of social relationships and social support networks and that it may have a negative impact on cognitive level. The effects of low socio-economic status, unhealthy living conditions that increase the risk of vascular disease, and a lack of medical care on dementia are still being debated (21). Just under eight percent of the AD group had a moderate economic situation, and no statistically significant relationship was found between economic situation and AD. In our study, it has been found that the frequency of AD is greater among manual laborers than others, and this was shown to be statistically significant.

Many studies have been conducted to explain the relationship between arterial hypertension and AD. In a long-term study conducted by Launer and associates, patients with hypertension were followed for 25 years. In this study, it was shown that hypertension is an independent risk factor for AD (18). The studies suggesting that there is no such relationship are generally sectional studies. Although HT is not a risk factor in some studies, it is reported that a history of high systolic and low diastolic blood pressures increases the risk of AD in some studies (22- 24). In our study, no statistically significant relationship was found between AH and HT.

Diabetes mellitus (DM) is one of the most common vascular diseases. The AH risk of type 1 DM is two times greater than that of type 2 DM. Recently, it was reported in sev-

eral prospective and cross-sectional study that the presence of DM is a risk factor for AD (25). The presence of DM was shown to be a risk factor for AH in Rotterdam and Mayo Clinic studies (22, 26). In our study, a statistically significant relationship was found between AH and DM.

The presence of cardio-vascular diseases and peripheral arterial diseases is shown to be a risk factor in the development of AD in the realized studies (27). In our study, in accordance with the literature, a statistically significant relationship was found between AH and heart diseases.

Dementia will occur after 20-30% of strokes in elderly people, and AH is responsible for 1/3 of those (14, 17). If the patient has history of cerebrovascular issues, this does not not mean that there is only vascular dementia. The patient has also Alzheimer's dementia. The presence of stroke is also an important risk factor for AH (28). In our study, a statistically significant relationship was found between AH and cerebrovascular diseases ($p<0.05$).

In Parkinson's disease clinics, there are serious deteriorations related to the cognitive functions. It is reported that Alzheimer's dementia and mild cognitive impairment increase in cases of Parkinson's disease (29). Many patients with Parkinson's disease are found to have Alzheimer's disease-related neuropathological changes upon autopsy. There appears to be some overlap in the neurodegenerative processes that occurs in Parkinson's disease and Alzheimer's disease, and the pathological processes may even be synergistic (30). In this study, a statistically significant relationship was found between AH and Parkinson's disease.

It is reported that hypothyroidism increases the risk of AH (31). In AH hippocampi, it was found that TSH-releasing hormone (TRH) concentrations were decreased. It has been suggested that TRH organizes the phosphorylation of proteins in the hippocampus and that it may play a role in the pathogenesis of AD (32). In our study, no statistically significant relationship was found between AH and thyroid diseases.

Some studies show a relationship between a history of psychiatric illness, cognitive impairment, and depression. In AH patients, depression is more pronounced in the early stages of the disease, although it is seen in all stages (10,16). The studies related to other psychiatric disorders and AH are not sufficient. No statistically significant relationship between AH and psychiatric disorders (depression, anxiety, or BZK) was found in our study group.

It was shown that in patients with a history of head trauma, AH risk was increased (33). In another study, those with head trauma were followed for nearly 40 years, and an increased risk of AD was not reported (14,17). In our study, there was also no a statistically significant relationship between AH and head trauma.

When the relationship between family history and AH was examined, it was reported that the presence of dementia in first-degree relatives, in parents or siblings, increased the risk of developing dementia 3-fold (14,17). A family history of Alzheimer's has been reported in more than 50 % of Alzheimer's disease cases that began before the age of 60. In at least half of the cases, this transition was found to be autosomal dominant (14,15,17). Although the genetic factors are more prominent and the transition is rare in early-onset AD, the role of family history and genetic regarding late-onset Alzheimer's disease, which occurs after the age of 60, remains debatable (34). The relationship between AH and a family history of dementia was found to be statistically significant.

There are studies that suggest the increased, decreased, and unchanged development of AH among smokers. It is reported that the rate of smoking is lower for Alzheimer's patients (35, 36). However, Euroderm, which is a prospective study, reported that AH is more common in those who are non-smokers (37). In our study, no statistically significant relationship was found between AH and smoking.

The relationship between alcohol use and AD is not conclusive. There are studies indicating that alcohol use protects against AH, but there are also studies indicating that alcohol use increases cognitive damage (38). In our study, no significant relationship was found between AH and alcohol use.

In our study, in accordance with the literature, it was seen that in those aged 65 and over, AH prevalence was 6.4% and that this rate was increased 17-fold with advanced age. In addition, the population of illiterate females over the age of 65 were about 5 times greater than the corresponding male population in our city center. In parallel with this, the number of female patients with Alzheimer's disease is approximately 2.5 times greater than the number of male patients in the model. These conditions are another factor that should attract attention. AH studies on the elderly are very few in number in Turkey. We believe that this study will suggest large-scale epidemiological studies related to AH that should be performed in the future.

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