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**Research Article** 

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# Clinical deterioration of Alzheimer's disease patients during the Covid-19 pandemic and caregiver burden

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#### Abstract

To investigate a possible deterioration of the symptoms of Alzheimer's disease (AD) patients during a quarantine period of 60 days, and the impact on caregiver burden. This study consisted of 54 individuals (36 female, 18 male) aged 60 years and over who had been diagnosed with AD. During the quarantine period, caregivers of the patients (child, spouse, relatives) who were confined to their homes were contacted by phone and administered a survey composed of questions for neuropsychiatric symptoms and caregiver burden. Patients' mean age was 77.18±6.96 years. The most worsening symptom was forgetfulness (35.2%) and agitation (24.1%). Incoherent speech, introversion, sleep disturbance, hallucinations, carry on with hobbies, reduced personal care, changes in appetite, and incontinence were less deteriorated. Of the caregivers, 61.1% thought that something terrible would happen to the patient, and 38.9% felt they could not find time for themselves. Drug rejection increased the burden twofold. Telemedicine methods, providing opportunities for the caregiver and the patient to walk outside, and giving medication that dissolves in the mouth or epidermal patches may be useful to prevent disease progression during the lockdown.

Keywords: Alzheimer's Disease; caregiver burden; Covid-19; neuropsychiatric symptoms; quarantine

# 1. Introduction

Alzheimer's disease (AD) is the most commonly seen type of dementia in persons aged 65 years and above (Alzheimer's Association et al., 2013). As the condition significantly affects activities of everyday life, the provision of care by a patient relative or a professional caregiver is required. The provision of caregiver continues for years and may cause psychological and physical problems for the carer. The size of the burden for the caregiver is directly proportional to the carer being female, having a low level of education, depression, social isolation, material problems, the lack of alternatives to being anyone else than the particular patient's carer, the severity of the patient's cognitive impairment, and the number of hours of care provided (Adelman et al., 2014; Yu et al., 2015).

The COVID-19 infection presents with greater severity in the older patient group (Li et al., 2020), and the mortality from pneumonia is high (Du et al., 2020). For this reason, in Turkey, as in the rest of the world, quarantine measures due to the COVID-19 pandemic continue to be applied mainly for the older age group. However, while trying to protect AD patients from the risk of infection, inevitably, new mental and physical problems arise. In a study by Lara et al. (2020) with a group of 40 AD patients, agitation, apathy, and a worsening of aberrant motor activity were observed over a five-week quarantine

period. In 30% of patients and 40% of carers, deterioration in the state of health was reported (Lara et al., 2020). Considering the uncertainty regarding drugs and vaccines, it is not yet possible to predict how much longer the COVID-19 pandemic will last. In this study, we aimed to establish possible deterioration of AD symptoms during a 60-day quarantine period among AD patients followed by our clinic and investigate the reasons for worsening and the burden for caregivers.

### 2. Materials and methods

Study participants were 54 persons aged 60 years and over (36 females, 18 males) with a diagnosis of AD according to DSM-IV-TR and NINCDS-ADRDA criteria. Approval of the ethic committee was obtained (10840098-604.01.01-e.19388). Patients with diagnoses of mixed-type dementia or other types of dementia were excluded. Patients' duration of education, the duration of AD, civil status, number of children, type of caregiver (child, spouse, relative, nurse), and sex of caregiver were recorded.

Caregivers of the patients who had stayed home during a 60-day quarantine (April 1<sup>st</sup>-May 30<sup>rd</sup> 2020) procedure were contacted by phone and administered a survey prepared by the

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neurology department of Medipol University Istanbul. All caregivers gave consent to participate the study. In the survey, the individuals caring for the patients were asked about deteriorating symptoms in 11 items (forgetfulness, rejection of medication, incoherent speech, agitation, introversion, sleep status, hallucinations, continued pursuit of their hobbies, personal hygiene, change in appetite, incontinence) for the last 2 months.

The caregiver burden was investigated with five questions:

Has the time you set aside for yourself diminished? Yes/No

- Do you have the wish to leave the patient and go away? Yes/No
- 2. Are you more irritable than you used to be? Yes/No
- 3. Are you worried that something terrible might happen to the patient? Yes/No
- 4. Do you feel your health being affected? Yes/No

Any "Yes" answer to these questions was given a score of 1 point, "No," a score of 0. The sum of points from this survey was calculated as the caregiver burden score.

The reason for deterioration for the last 2 months during the quarantine procedure was investigated with five items:

- 1- I could not procure the medication for AD.
- 2- I was left to my own, could not call anyone for help in this period.
- 3- I could not take the patient to the doctor for a check-up.
- 4- I used to go out regularly with the patient, could not go out in this situation
- 5- I am agitated because COVID-19 can affect the patient.

# 2.1. Statistical analysis

Data were assessed using IBM SPSS Statistics, Version 25.0. In the evaluation of descriptive data, frequency, percentage, mean, standard deviation, and minimum-maximum values were used. Categorical variables were evaluated with chi-square analysis. In the evaluation of binary and non-parametrically distributed mean scores, the Mann-Whitney U test was used. A value of p<0.05 was considered statistically significant. To evaluate the effect of variables on the mean caregiver burden scores, a linear regression model was built with the variable that was significant in the preliminary analysis.

#### 3. Results

Patients' mean age was 77.18±6.96 (60-94) years, mean duration of education 6.01±4.74 (0-18), and mean duration of illness 3.83±2.78 (1-14) years. Thirty persons were married, 24 were widowed. The average number of children was 3.77±0.50 (0-13). Of all patients, 72.2% received care from their child, 14.8% from their spouse, and 13.0% from another relative (nephew/niece, daughter-in-law). Sixty-three percent of the caregivers were female, 37% were male.

Before the quarantine, six patients (11.1%) had refused medication, 23 persons (42.6%) had been talking incoherently, 28 (51.9%) had shown agitation, 26 (48.1%) introversion, 23 individuals (42.6%) sleep disorder, 13 (24.1%) hallucinations, 24 persons (44.4%) were unable to pursue their hobbies, 14 individuals (25.9%) had issues with personal care, 24 (44.4%) had a change in appetite, and 22 patients (40.7%) were incontinent.

These are the rates of deterioration in clinical findings during the quarantine period:

Worsening of forgetfulness was reported for 19 persons (35.2%), two persons (3.7%) had more severe drug compliance problems, nine individuals (16.7%) spoke more incoherently, 13 patients (24.1%) were more agitated, 11 persons (20.4%) more introverted, 8 (14.8%) suffered sleep disturbance, seven (13.0%) had hallucinations, 5 (9.3%) could not carry out their hobbies, 2 (3.7%) showed reduced personal care, 9 (16.7%) had less appetite, and 6 (11.1%) had more problems with incontinence.

Of the caregivers, 27 (50.0%) felt they could not find time for themselves, 8 (14.8%) wished to leave the patient and go away, 21 (38.9%) said they were irritable, 33 (61.1%) expressed their fear that something terrible would happen to the patient, and 17 (31.5%) felt their health had suffered. In the range between 0 and 5 points, the average caregiver burden score was  $1.98\pm1.38$ .

Regarding the reasons for deterioration:

- 1- I could not procure the medication for AD: 0 (0.0%)
- 2- I was left to my own, could not call anyone for help in this period: 1 (1.9%)
- 3- I could not take the patient to the doctor for a check-up: 3 (5.6%)
- 4- I used to go out regularly with the patient, could not go out in this situation: 18 (33.3%)
- 5- I am agitated because COVID-19 can affect the patient: 2 (3.7%)

While a lower rate of deterioration in the pursuit of hobbies was found for patients who were cared for by their children (p=0.003), no statistically significant relationship was found between degrees of relationship and deterioration in clinical characteristics (p>0.05 in each category).

Caregiver burden scores were significantly higher in the case of patients refusing to take their medication (p=0.035). For other clinical characteristics, caregiver burden scores were similar between patients who showed deterioration and those who did not (p>0.05 in each category).

In the linear regression model using the only variable to be significant in binary analyses, it was found that rejection of drugs increased the caregiver burden score about two-fold.

Table 1. Distribution of degrees of relationship for caregivers by state of deterioration of patients' clinical status

		Carer child n (%)	Carer spouse n (%)	Carer other relative n (%)	Test value χ <sup>2</sup> ; p	
Forgetfulness	No deterioration	24 (61.5)	5 (62.5)	6 (85.7)	1.543; 0.462	
	Deterioration	15 (38.5)	3 (37.5)	1 (14.3)		
Drug rejection	No deterioration	38 (97.4)	8 (100.0)	6 (85.7)	2.648; 0.266	
	Deterioration	1 (2.6)	0(0.0)	1 (14.3)		
Incoherent speech	No deterioration	32 (82.1)	7 (87.5)	6 (85.7)	0.175; 0.916	
	Deterioration	7 (17.9)	1 (12.5)	1 (14.3)		
Agitation	No deterioration	31 (79.5)	6 (75.0)	4 (57.1)	1.625; 0.444	
	Deterioration	8 (20.5)	2 (25.0)	3 (42.9)		
Introversion	No deterioration	31 (79.5)	7 (87.5)	5 (71.4)	0.596; 0.742	
	Deterioration	8 (20.5)	1 (12.5)	2 (28.6)		
Sleeping status	No deterioration	35 (89.7)	7 (87.5)	4 (57.1)	5.038; 0.081	
	Deterioration	4 (10.3)	1 (12.5)	3 (42.9)		
Hallucination	No deterioration	34 (87.2)	8 (100.0)	5 (71.4)	2.704; 0.259	
	Deterioration	5 (12.8)	0(0.0)	2 (28.6)		
Hobbies	No deterioration	38 (97.4)	7 (87.5)	4 (57.1)	11.585; 0.003	
	Deterioration	1 (2.6)	1 (12.5)	3 (42.9)		
Personal hygiene	No deterioration	38 (97.4)	8 (100.0)	6 (85.7)	2.648; 0.266	
	Deterioration	1 (2.6)	0(0.0)	1 (14.3)		
Appetite	No deterioration	33 (84.6)	6 (75.0)	6 (85.7)	0.475; 0.789	
	Deterioration	6 (15.4)	2 (25.0)	1 (14.3)		
Incontinence	No deterioration	33 (84.6)	8 (100.0)	7 (100.0)	2.596; 0.273	
monument	Deterioration	6 (15.4)	0(0.0)	0(0.0)	2.570, 0.275	

Table 2. Distribution of caregiver burden scores according to deterioration of patients' clinical characteristics

		n (%)	Total caregiver score mean±SD (min-max)	Test value Z; p	
Forgetfulness	No deterioration	35 (64.8)	$1.80 \pm 1.41 \ (0.00 - 5.00)$	1.374; 0.170	
	Deterioration	19 (35.2)	2.32±1.29 (0.00-4.00)		
Drug rejection	No deterioration	52 (96.3)	$1.90\pm1.35\ (0.00-5.00)$	2.065; 0.035	
	Deterioration	2 (3.7)	4.00±0.00 (4.00-4.00)		
Incoherent speech	No deterioration	45 (83.3)	$1.89 \pm 1.40 \ (0.00 - 5.00)$	1.154; 0.249	
	Deterioration	9 (16.7)	$2.44 \pm 1.24 \ (1.00 - 4.00)$		
Agitation	No deterioration	41 (75.9)	1.95±1.36 (0.00-5.00)	0.280; 0.780	
	Deterioration	13 (24.1)	2.08±1.50 (0.00-4.00)		
Introversion	No deterioration	43 (79.6)	1.98±1.46 (0.00-5.00)	0.122, 0.905	
	Deterioration	11 (20.4)	2.00±1.10 (1.00-4.00)	0.132; 0.895	
Sleeping status	No deterioration	46 (85.2)	2.07±1.44 (0.00-5.00)	0.986; 0.343	
	Deterioration	8 (14.8)	1.50±0.93 (0.00-3.00)		
Hallucination	No deterioration	47 (87.0)	1.89±1.37 (0.00-5.00)	1.240; 0.232	
	Deterioration	7 (13.0)	2.57±1.40 (1.00-4.00)		
Hobbies	No deterioration	49 (90.7)	1.92±1.37 (0.00-5.00)	1.040; 0.321	
	Deterioration	5 (9.3)	2.60±1.52 (1.00-4.00)		
Personal hygiene	No deterioration	52 (96.3)	1.98±1.35 (0.00-5.00)	0.961; 0.981	
	Deterioration	2 (3.7)	2.00±2.83 (0.00-4.00)		
Appetite	No deterioration	45 (83.3)	1.96±1.45 (0.00-5.00)	0.416; 0.677	
	Deterioration	9 (16.7)	2.11±1.05 (1.00-4.00)		
Incontinence	No deterioration	48 (88.9)	$1.90\pm1.36\ (0.00-5.00)$	1.283; 0.216	
	Deterioration	6 (11.1)	2.67±1.51 (1.00-4.00)		

**Table 3.** Linear regression model showing the effect of changes in patients' clinical characteristics on caregiver burden score

	B (95% Cl)	t	Sig.
Rejection of medication (binary)	2.096 (0.167- 4.025)	2.181	0.034
(Constant)	1.904 (1.533- 2.275)	10.292	0.000

#### 4. Discussion

In our study, which included AD patients in the early-to-intermediate stage of the disease, neuropsychiatric symptoms were seen in the foreground. Before the quarantine, the most common symptom had been agitation (in about half the patients); issues about carrying on with their hobbies and appetite problems had also been common. Insomnia, incoherent speech and incontinence were found in 40% of patients. As patients with these symptoms remained isolated in

their homes together with their caregivers during quarantine, we investigated how this situation affected the course of AD and the burden on caregivers. The most significant change in patients was an increase in forgetfulness (35.2%), while deterioration of agitation symptoms (24.1%) was found in second place. Incoherent speech, introversion, rejection of medication, and sleep problems also deteriorated in one-fifth of patients. The deterioration in continuing with their hobbies was significantly lower in patients receiving care from their child compared to patients with other caregivers. Reasons for this observation may include the younger age of the patient's child compared to their spouse and the child's more considerable attention in comparison with other family members.

Studies by Peters et al. (2015) showed agitation and psychotic symptoms to be the most relevant predictors for the progression of dementia. Increased agitation and forgetfulness caused by the lack of opportunities to leave the house during quarantine may have led to the deterioration of all other symptoms. There are only a limited number of studies on this issue found in the literature. Research by Boutoleau-Brotonniere et al. (2020) with 38 AD patients quarantined for two months during the COVID-19 pandemic found deteriorating neuropsychiatric symptoms and a significant increase in forgetfulness in 10 individuals (26.3%); however, they showed this situation not to be correlated with caregivers' stress and the duration of the quarantine. In a study by Lara et al. (2020), five weeks of quarantine AD patients showed significant deterioration only in agitation, apathy, and aberrant motor activity, while no significant deterioration was found in neuropsychiatric symptoms like appetite, hallucinations, anxiety, and depression.

Physical activity is known to improve cognition (Jia et al., 2019) and neuropsychiatric symptoms in AD patients (Hoffmann et al., 2016). Remarkably, when we asked caregivers about the etiology of the reasons for patients' deterioration, they most commonly (33.3%) attributed the observed deterioration to the impossibility of taking the patients out for walks. We found no problems with the provision of drugs, nor did being on their own or not being able to take patients to medical check-ups cause concerns, and patient relatives were not overly worried about COVID-19, either.

Considering these aspects one by one, potential problems with drug procurement had been prevented by measures of the Turkish Ministry of Health facilitating the provision of medication to chronically ill patients during the pandemic. Due to COVID-19 infection risk, restrictions were applied to relatives and friends other than the caregiver visiting patients at home (Azarpazhooh et al., 2020), which may have caused carer and patient to feel even more lonely. However, in our study, only one person included this aspect among the reasons for the deterioration in the patient's symptoms. As for all

persons living with a chronic illness, medical check-ups and management of pharmacotherapy are essential for AD patients, too. Nevertheless, only 5% of the caregivers considered the impossibility of seeing a doctor for check-up over two months during the pandemic a cause for deterioration.

COVID-19 affects mental health in 25% of the population (Choi et al., 2020). In a study in Turkey, the rate of anxiety during the COVID-19 pandemic increased to around 45% (Özdin and Bayrak Özdin, 2020). Government advice to stay home because of COVID-19 may cause increased stress, depression, and anxiety rates in society (Ozamiz-Etxebarria et al., 2020). However, patient relatives participating in our study reported a relatively low proportion of stress and anxiety (3.7%).

Caring for AD patients is difficult due to the progressive course of the disease and the presence of neuropsychiatric symptoms (Germain et al., 2009). Factors increasing the caregiver's burden have been researched in earlier studies. Anxiety, agitation, disinhibition, aggressive behavior, sleep problems, the carer being female and the patient's spouse, and social isolation are among the factors that contribute most to an increase in the carer's load (Isik et al., 2019). While a study made in care homes found emotional exhaustion in 25% of caregivers (Yıldızhan et al., 2019), this rate increased to 40% when care was provided by a family member (Truzzi et al., 2012). Many adult children in Turkey caring for their parents suffering from AD feel a responsibility towards their parents, do not trust care homes, and prefer providing care themselves (Ar and Karanci, 2019). In our study, around 63% of caregivers were female; 72% were children and 14% spouses. There was no caregiver who was not related to the patient. All of the caregivers had spent the 60 days in social isolation in their homes together with the patient.

Our study found that the disease progressed faster than expected and we also investigated the disease-related caregiver burden in addition. Half of the caregivers stated not to have enough time for themselves during the pandemic, while 61% expressed their worries that something terrible might happen to the patient. Around one-third of caregivers felt more irritable, and again one-third observed that their health had been affected. During this period, only eight persons expressed a wish to leave the patient and go away. The only parameter for an increase in the burden of care that we could establish was a lack of compliance with medication (twofold).

Among the limitations of our study are the inability to administer detailed neuropsychiatric tests before and after the pandemic, the impracticability of carrying out more detailed surveys to investigate the caregiver burden over the phone, and a low number of patients in our sample. Also we cannot obtain the information about the drugs of the patients as anti-dementia drugs and antipsychotic medication can affect the symptoms positively.

During a 60-day quarantine period, the symptoms most commonly found to deteriorate in AD patients were forgetfulness and agitation. In the caregivers' opinion, the most critical reason for deterioration was the impossibility of going out for walks. The caregiver burden increased during this period, mainly due to patients' problems being persuaded to take their medication more than other commonly seen neuropsychiatric symptoms.

The more frequent use of telemedicine through digital devices may help monitor neuropsychiatric symptoms of patients with dementia in general, not only during a pandemic, to solve problems that may emerge in the context of the disease (Cuffaro et al., 2020). Other contributions to addressing these issues might include allowing patients to go out at certain times, finding ways to reduce the caregivers' load, and prescribing medication that dissolves in the mouth or epidermal patches rather than tablets that may be hard to swallow

#### **Conflict of interest**

None to declare.

## Acknowledgments

None to declare.

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